

ALKALI CATION BINDING TO NONIONIC POLYMERS

By

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ALKALI CATION BINDING TO NONIONIC POLYMERS

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Major Department: Chemistry

The alkali cation binding of nonelectrolyte polyether type polymers in several nonaqueous solvents was measured by viscometric, spectrophotometric, potentiometric and conductance techniques. An attempt was made to correlate these findings to the ability of those polymers to catalyze nucleophilic substitution reactions to acetate salts with n-butyl bromide.

UV-visible studies indicated that the complexation of sodium salts to polyethers in chloroform increased with increasing chain length up to tetraglyme, which contains five oxygen atoms. Further increase in chain length had no apparent effect on the complexing power of the polyethers. Viscometric and potentiometric studies indicated that in these systems many cations were bound to a single high molecular weight chain. These studies also

showed that cation binding initially led to chain expansion due to chain bound cation-cation repulsion. Addition of more salt, however, gave a reduction in viscosity as more anions within the polymer domain shielded the positive charges. From conductance results it was shown that the number of cations bound per chain increased with increasing molecular weight. Further addition of polymer led to a redistribution of cations from polymer chains containing more than one cation to chains containing no cations. Binding of cations was strongest in THF, followed by acetonitrile, and acetone. Binding constants were calculated for the complexation of NaBPh_4 to PEO 1000 and PEO 6000 in acetonitrile. Distribution equilibria were used to study the interaction between alkali cations and poly(acryloyltyrocidine), a polymer containing a cyclic antibiotic. It was found that the ion selectivity of the polymer was similar to that of tyrocidine itself.

The effect of poly(ethylene oxide) and similar polymers in the phase-transfer reaction of sodium and potassium acetate with n-butyl bromide in acetonitrile was investigated as well as the corresponding homogeneous reaction in 5% H_2O /95% CH_3CN (v/v) medium. In both cases a correlation was found between the complexing abilities and catalytic efficiencies of the lower molecular weight polyethers, although the effects were more pronounced

in the phase-transfer reactions. Polyethers of molecular weight 600 and 1000 were found to be the most effective catalysts, the reaction yields decreasing as the molecular weight increased to 6000 and beyond. The smaller differences with the various polymers in homogeneous media were probably due to the effect of water on anion nucleophilicities and cation coordination. In heterogeneous media the differences may have been due to a higher efficiency in transport of salt from the crystal into the solution phase, a less efficient complexation of salt by higher molecular weight polymers, or a combination of these effects.

CHAPTER I

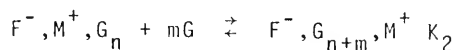
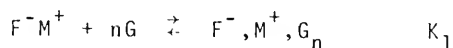
INTRODUCTION

The complexation of alkali cations by neutral or nonionic molecules is a phenomenon which has been extensively studied. Depending on such factors as cation size and charge, the size, shape and distance of the negative counterion, the ability of the solvent to solvate either or both of the ions, the nature of the binding site, and the temperature, the degree of binding may vary over a wide range.

Monomeric Complexing Agents

A series of polyglycol dimethyl ethers or glymes of the general formula $\text{CH}_3\text{O}(\text{CH}_2\text{CH}_2\text{O})_x\text{CH}_3$ was investigated with respect to their behavior in solvating alkali cations.^{1,2} It was found for compounds ranging from $X = 1$ to $X = 6$ that coordination complexes were formed with lithium, sodium, and potassium salts of fluorenyl carbanions in low dielectric constant solvents. The complexation of these salts with glyme led to contact ion pairs, glyme-separated ion pairs, or to a mixture of both depending on the size of the cation and the chain

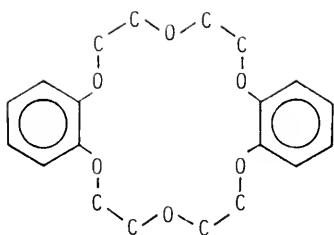
length of the glyme. By adding different quantities of glyme to fluorenyllithium in dioxane or fluorenylsodium in tetrahydrofuran (THF), it was possible to measure the equilibrium constants of the reaction



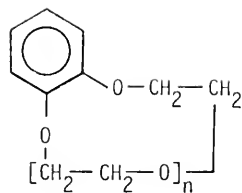
where n and m are the number of glyme molecules participating in the complexation, F^{-},M^{+},G_n is the contact ion pair, and F^{-},G_{n+m},M^{+} is the solvent separated ion pair. As the number of oxygens in the chain increased, the various complexation constants increased up to an X value of three for lithium and four for sodium where they leveled off. Temperature dependence studies indicated that glymes were more effective than solvents such as tetrahydrofuran in coordinating alkali ions due to a smaller loss in entropy. This small entropy loss is expected because one glyme molecule contains several oxygen atoms all of which may coordinate with a cation of appropriate size, whereas several THF molecules would be needed to occupy the same coordination sites. It has also been shown that crystalline 1:1 complexes of $NaBPh_4$ were obtained with glymes having $X = 4, 6$, and 7 as well as a 2:1 complex with the compound having $X = 3$.³

The effect of the small entropy loss on binding observed in the polyglycol dimethyl ethers was even more pronounced in the macrocyclic polyethers, or crown ethers, first described by Pedersen in 1967. These compounds are cyclic in nature composed of repeating $(-O-CH_2-CH_2-)_n$ units (see Figure 1). In these molecules the coordinating oxygen atoms are positioned for favorable complexation of an ion of suitable size. On cation binding, little entropy loss is experienced. Containing a central hydrophilic cavity with a hydrophobic exterior, these crown ethers were shown to solubilize certain alkali cation salts in aromatic or chlorinated hydrocarbons. These complexes as well as those of the polyglycol dimethyl ethers were believed to be due to ion-dipole interactions between the cation and ether oxygens.^{4,5}

Frensdorff further studied the stability constants of these complexes by potentiometry using cation-selective electrodes. Due to water's stronger solvation of the cation, he found the binding constants in methanol to be significantly higher than in water. Also, as the ring size varied, cation selectivity changed so that an individual crown ether would most efficiently bind the cation which would just fit into the center cavity. The complexation of large cations by polyethers having small cavities was increased in several instances by the formation of a 2:1 crown-cation complex. Replacing the oxygens with

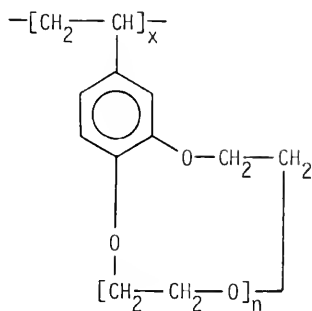


Dibenzo-18-Crown-6



18-Crown-6

$$n = 4$$



Poly(vinylbenzo-15-Crown-5)

$$n = 3$$

Figure 1. Typical Crown Ethers

nitrogen or sulfur weakened the complexing ability toward alkali cations.⁶ Furthermore, Frensdorff quantitatively described the ability of crown ethers to extract alkali salts from an aqueous layer into a nonaqueous layer containing the crown ether.⁷

Following these initial studies, an extremely large number of multidentate macrocyclic compounds was synthesized. These included cyclic polyethers, alkyl and aromatic substituted cyclic ethers, macrocycles containing nitrogen donor atoms, sulfur donor atoms and mixed donor atoms. In almost every case, these compounds were shown to complex one or more cations and were usually specific for a particular cation.⁸

Crown-complexed salts generated substantial interests due to their ability to exist as separated ion pairs in solution.⁹ Takaki, Hogen Esch and Smid studied the optical spectra of crown ether complexed fluorenylsodium and fluorenylpotassium in tetrahydrofuran and tetrahydropyran (THP). The salts were shown to exist as a mixture of contact and crown-separated ion pairs, the stability of the complexes being a function of temperature, solvent, size of the cation and structure of the crown compound.¹⁰

The cyclic ligand concept was extended in a series of macroheterobicycles called cryptates, designed by Lehn.¹¹⁻¹⁴ As a result of their three-dimensional cage structures, which allow cations to be included within the

central molecular cavity, these compounds exhibited binding constants even greater than the crown ethers. Difficult synthetic procedures and relative unavailability have limited their use at this time.

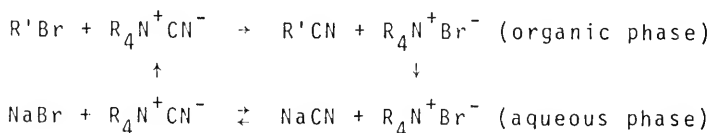
Another group of compounds which complex with alkali ions is called the ionophores. These are antibiotics which form lipid soluble complexes with alkali metal salts and then transport these ions across lipid barriers including artificial biological membranes. Having a cyclic peptide structure, the ionophores complex cations by ion-dipole interaction with carbonyl or ether oxygens. The oxygens replace all or some of the solvent molecules in the solvation sphere of the aqueous ions. The complex then assumes a conformation in which the charged cation is held in the center of the ionophore while alkyl groups form a hydrophobic outer surface allowing the entire molecule to pass through the low dielectric environment of lipid membranes.^{15,16} This ability to transport ions through membranes has also been demonstrated by crown ethers.¹⁷

Many antibiotics have been shown to complex cations and transport them through cell mitochondria. Among these are certain depsipeptides, macrotetralides, and polypeptides including valinomycin, the macrotetralide actins, the enniatins, and the gramicidins; and also monocarboxylic polyethers, including nigericin,

dianemycin, the monesins, X-206 and X-537.^{16,18} Various methods have been used to study the binding strength and selectivity of various antibiotics. Extraction of cations from an aqueous layer into a nonaqueous layer containing the antibiotic was used in some of the initial studies.^{15,19} Other methods used included measuring the change in conductance across lipid membranes due to antibiotic modified cation transport,^{20,21} ion-selective electrodes,¹⁹ circular dichroism,²² and fluorescence spectroscopy.^{22,23,24} As a result of these and other studies, a striking resemblance between antibiotics and certain crown ethers was noticed in their selectivity toward cations. It was then realized that crown ethers could serve as model compounds for the large cyclic antibiotics in examining the processes involved during cation transport in the mitochondria.²⁵

The property of various ligands, particularly crown ethers, which enables them to solubilize salts in nonpolar media and to decrease the cation-anion interaction in ion pairs has resulted in their use as catalysts in synthetic reactions. The process of phase-transfer catalysis was first investigated by Starks in the displacement reactions of alkyl halides in an organic phase with inorganic ions in an aqueous phase.²⁶ Although these reactions are initially inhibited because of phase separation, they were catalyzed by small amounts of organic soluble tetraalkyl ammonium or tetraalkyl phosphonium

salts. This process was believed to involve the complexation of nucleophilic cyanide anions in the aqueous phase by quaternary cations and the subsequent transfer of these ions into the organic phase. Here the cyanide anions reacted with the alkyl substrates displacing halide ions. The halide ions were then complexed by the quaternary cations and carried into the aqueous layer. Replacement of the halide ion by another nucleophilic cyanide anion led to further phase-transfer catalysis. The reaction between sodium cyanide and 1-bromooctane may be described as follows:



The nucleophilic displacement reactions have also been carried out in two phase organic-aqueous systems using various alkyl mesylates and halides as substrates with crown ether-complexed alkali halides as nucleophiles.²⁷ The limitation of quaternary ammonium or phosphonium catalysts was that they must generally be used only with the transfer of ions from an aqueous phase into nonpolar solvents. However, crown ethers have the ability to promote a direct solid-liquid phase-transfer of salts into nonpolar solvents. Liotta demonstrated that in benzene

or acetonitrile, 18-crown-6 could complex potassium fluoride, acetate, cyanide, or azide which in turn would partially free the anion to act as a strong nucleophile toward alkyl halides.²⁸⁻³¹ In a similar study, Zubrick, Dunbar, and Durst examined the reaction of benzyl chloride with potassium cyanide in acetonitrile containing 18-crown-6. They found 90-95% reaction and even when 1-2% water was added, they still achieved an 85-95% yield.³² Other investigations have shown that crown ether-complexed KMnO_4 in benzene could oxidize olefins, alcohols, and aldehydes;³³ and aromatic hydrocarbons containing acidic hydrogens (e.g., fluorene) could be alkylated by reaction with aqueous sodium hydroxide in the presence of dibenzo-18-crown-6.³⁴

The effectiveness of crown ethers as reagents for solid-liquid phase-transfer reactions can be attributed to their powerful cation binding ability and the fact that they are flexible molecules with several polar sites.³⁵ Their flexibility allows the crown ethers to interact with the surface of a crystal lattice of a salt in the most energetically favorable geometry. By assuming the same shape as the surface of the crystal lattice, the crown ether can readily transfer a cation from its lattice site to the crown ether cavity. The anion remains as an ion pair with the cation complex.

Polymeric Complexing Agents

The complexes which have been described up to this point involve low molecular weight species where the ligand usually functions in a 1:1 relationship with the alkali cation. With polymeric complexing agents, however, several ions or ion pairs may be bound to one polymer molecule. In addition to the entropy effects mentioned for glymes and crown ethers, other effects are also present in the binding of cations to nonionic polymers. One effect is polymer conformation which determines the proximity of binding sites to one another and, therefore, has a direct effect on the binding process. As ions become bound along the polymer chain, the polymer becomes in effect a polyelectrolyte. The cation binding may then be reduced due to charge repulsions by cations already bound to the chain. The repulsions may be decreased by counterions in the vicinity of the polymer shielding the charges.³⁶ Other factors may involve dipole-dipole interactions in the polymer domain between ion pairs on the chain and ion pairs in solution. These factors may increase or decrease ion binding to the polymer. The effects listed above are quite complicated and are not well understood.

These effects were studied with poly(ethylene oxide), the polymeric analog of the previously mentioned glymes. Viscosity studies by Lundberg, Bailey, and

Callard showed that 0.05 M potassium fluoride added to 2% poly(ethylene oxide) in methanol resulted in the binding of 1 potassium fluoride molecule per 9 ethylene oxide repeating units.³⁷ Liu noted cooperative effects in an NMR study of the binding of potassium iodide to poly(ethylene oxide) in methanol. The polymeric type interaction began with the oligomer having seven repeating units.³⁸ Another approach involved visible spectroscopy of alkali metal fluorenyls complexed to poly(ethylene oxide). Here again, the strongest complex was formed at an ethylene oxide unit to metal ion ratio of approximately 5:1 for sodium and 7:1 for potassium.³⁹

Further examples of polymeric cooperative effects were demonstrated by Smid with the syntheses and cation binding studies of poly(vinyl crown ethers). Using optical spectroscopy, distribution equilibria, conductance, viscosity and ion transport through liquid membranes, he was able to compare the cation binding properties of polymers containing pendant crown ether ligands with crown ethers themselves. In most cases, the crown ethers which formed 1:1 crown-cation complexes demonstrated equal to slightly better binding of cations in the polymeric form. However, for those crown ethers capable of forming a 2:1 crown-cation complex the complexation constants for the polymeric crown ethers were considerably enhanced over the monomeric species.⁴⁰⁻⁴⁴

The polymeric cooperative effect is apparent not only with cation binding but also with increased reaction rates where polymeric materials serve as catalysts. It has been shown that the Williamson reaction between sodium phenoxide and butyl bromide in dioxane occurred over 100 times faster in the presence of poly(vinyl pyrrolidone) as in a solution containing the same concentration by weight of N-methyl pyrrolidone.⁴⁵ Here the rate enhancement was attributed to the dissociation of sodium phenoxide based on the tight solvation of sodium cations by pyrrolidone segments in the polymer coil. From entropy considerations, it would be a lower energy process to solvate a sodium cation with pyrrolidone groups attached to a polymer than with free pyrrolidone residues. This should lead to higher rates with polymeric catalysts.

Objectives

Catalysis of synthetic reactions by polymers is of both practical and theoretical interest. Polymers may be relatively easily retrieved from homogeneous reaction mixtures by various means which would allow their reuse as catalysts. Polymers may also catalyze reactions in heterogeneous fashion in the form of microporous beads or gels which would immobilize the polymer in the solid state. Here again, separation from the reaction mixture

is easily achieved. As mentioned previously, polymers have the ability to complex cations through a variety of effects. Frequently such complexations are as strong or stronger than with the corresponding low molecular weight analogs. Polymers, in addition, may exist in conformations which would possibly allow complexing sites to interact with solid phase reagents in a more energetically favorable manner than low molecular weight compounds.

In spite of these advantages of polymer catalysts, there have not at this time been many reported investigations of polymers in phase-transfer reactions. Phase-transfer catalysts may serve a dual role. They may not only transfer a reactive substance, usually a salt, from a solid or aqueous phase into an organic layer, but they may also modify this reactant once it is in the organic phase to increase its reactivity. How this is done, however, has not been clarified in detail.

It is believed that by studying cation binding and catalytic properties of a series of phase-transfer catalysts of varying degrees of polymerization, more insight may be obtained in the nature of the phase-transfer process of both low and high molecular weight compounds. It would also be of interest to study the correlation of the cation binding and catalytic properties of various other polymers in order to assess the role of various cation complexing sites. Such studies may be of

help in clarifying the nature of polymer catalysis in phase-transfer reactions since at least for solid-liquid phase-transfer processes, the nature of the catalysis is not well understood.

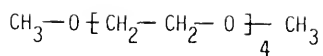
Therefore, the objectives of this research project were as follows:

1. Study the ability of various nonionic polymers, having similar binding sites but differing in the location of these sites, to bind alkali cations and to modify the ion pair structure of their salts. This was done by conductance and visible spectroscopy.
2. Study the phase-transfer ability of these polymers as a function of molecular weight, polymer concentration, and solvent composition.

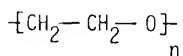
The polymers chosen for the phase-transfer catalysis work were ethers. Poly(ethylene oxide) which contains ether oxygens in its backbone was readily available in various molecular weights. Various glymes, low molecular weight analogs of poly(ethylene oxide), were also commercially available. The vinyl glyme 3,6,9,12,15-pentaoxa-1-heptadecene containing a pendant group with five ether oxygens was commercially available, easily polymerized, and the polymer was soluble in most common solvents.

This material in polymer form was investigated and compared to the previously listed ethers. Examples of the polyethers are given in Figure 2.

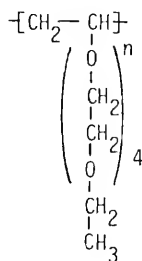
Most common cyclic antibiotics which were known to bind cations had no suitable functional group to aid in attachment to a polymer or the group present was involved in cyclization of the antibiotic during the complexation process.^{15,16,18,19,21,46,47,48} The cyclic antibiotic tyrocidine contained the ornithine amino acid function which included a primary amine group, facilitating attachment to a polymer chain. Also, tyrocidine bound alkali cations, particularly sodium, and it was also commercially available.⁴⁹ Therefore, the antibiotic tyrocidine met the selected criteria, was attached to a polymer, and was used in the study of alkali cation binding to various polymers. The antibiotic structure is given in Figure 3.



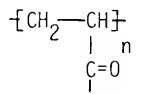
Tetraglyme



Poly(ethylene oxide)



Poly(3,6,9,12,15-pentaoxa-1-heptadecene)

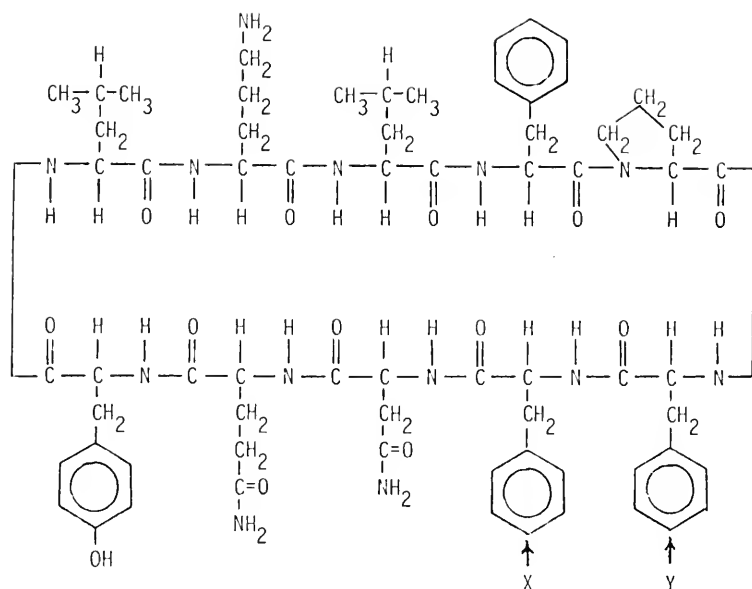


Tyrocidine

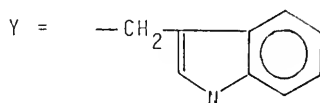
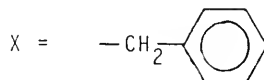
Poly(acryloyltyrocidine)

Figure 2. Cation Complexing Agents

Tyrocidine A



Tyrocidine B



Tyrocidine C

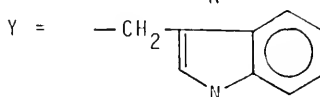
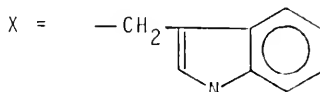


Figure 3. The Antibiotic Tyrocidine

CHAPTER II

CATION BINDING

Many different techniques have been used to study the complexation of cations to nonionic ligands. The vibrations of alkali cations encaged by crown ethers in solution have been examined by far infrared spectroscopy.⁵⁰ In this region, solvent- and anion-independent bands were used to determine the effects on the cation motion frequencies in solution caused by ion binding. Proton and ^{23}Na magnetic resonance have been used to study the chemical shifts induced when a cation is coordinated to a cyclic ether.^{51,52} Also, calorimetry has proved useful in determining binding constants as well as enthalpy and entropy values for cation complexation.^{53,54} Another valuable tool for calculating binding constants was potentiometry with cation-selective electrodes.⁶ This measured the number of free ions remaining in solution after a ligand had been added. The use of alkali cation salts of fluorescent probes or even the fluorescent thallium cation itself made possible the use of fluorescence spectroscopy in the study of cation binding to various ligands, particularly cyclic antibiotics.^{23,24} In polymer systems, light scattering and viscosity have

been used to examine the polyelectrolyte effect of chain expansion upon binding of cations along the polymer chain.^{36,37} Distribution equilibria have been useful in demonstrating the ability of monomeric or polymeric complexing agents to extract alkali cation salts from an aqueous phase into an organic layer where the salt would normally be insoluble.^{4,7,18,21,42} An alternative to studying parameters directly concerned with the cation was to study the UV-visible spectra of salts with anions such as picrate or fluorenyl. These salts were sensitive to changes in the interionic ion pair distances caused by complexation of the cation, making them valuable probes of the binding strength of various ligands.^{55,56} Another method which has been used to determine binding constants as well as the stoichiometry of the cation complex is conductance.^{43,57} In solvents where the alkali cation salts existed as free ions, the conductance of the solution was shown to decrease upon addition of ligands such as crown ethers as long as the mobility of the complexed ion was lower than that of the noncomplexed ion. This decrease continued until nearly all the cations were complexed. At this point the conductance began to level off with the breaking point yielding the stoichiometry of the complex. In the present study, the following techniques were used: viscosity, distribution equilibria on one polymer which had the appropriate solubilities,

cation-selective electrodes, UV-visible spectroscopy, and conductance.

Results

Viscometry

Lundberg, Bailey, and Callard examined the effects on viscosity of adding alkali metal halides to poly(ethylene oxide) solutions in methanol.³⁷ They observed high viscosity with moderately high salt concentration (0.02 M potassium iodide) with a decrease in viscosity upon further addition of salt. From their results, they calculated that one molecule of salt associated with approximately nine ethylene oxide units. The anion was tentatively postulated as the species directly bound to the polymer. The present study expanded that of Lundberg et al., particularly to lower salt concentrations and different cations, to further investigate the polyelectrolyte effects caused by binding cations along the polymer chain, as well as to elucidate the actual ion complexed to the polymer.

To a methanol solution containing 2.5×10^{-2} M in monomer of poly(ethylene oxide) of molecular weight 6×10^6 g/mole was added potassium bromide over a concentration range of 1.0×10^{-4} M to 1.0×10^{-1} M. The results are shown in Figure 4. Initial additions of KBr

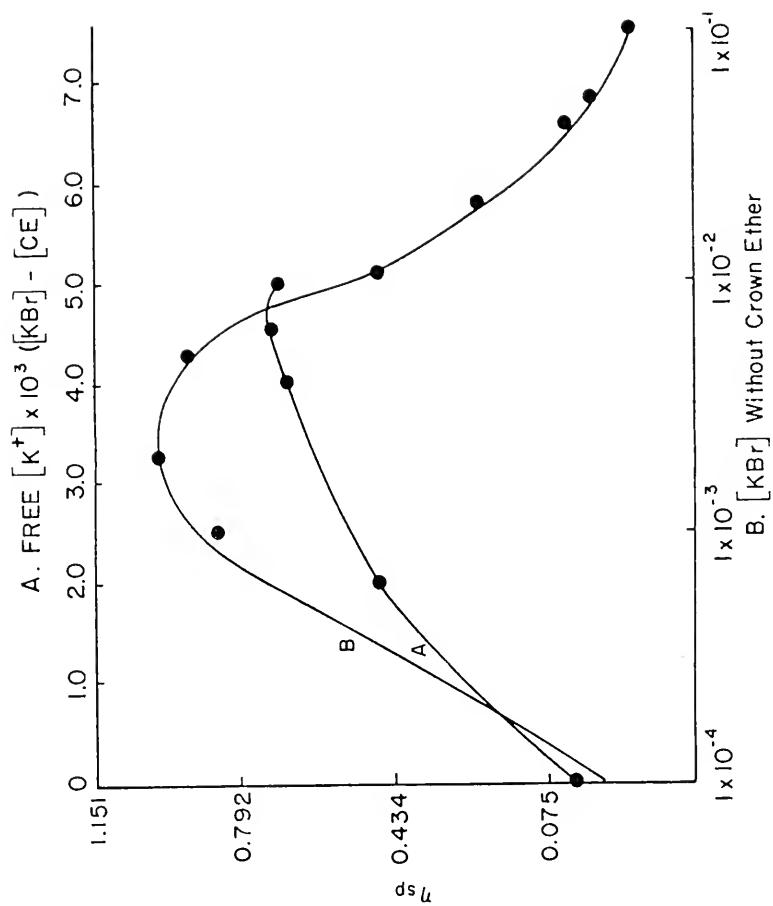


Figure 4. Viscosity of PEO with KBr Added

are followed by an increase in viscosity. Here, cations which we proved to be bound along the polymer backbone were involved in charge-charge repulsions, expanding the chain and increasing the viscosity. However, after passing through a maximum at 2.5×10^{-3} M KBr, the viscosity began to decrease. The further addition of salt led to a viscosity decrease caused by counterion shielding. Division of the concentration of monomer units of poly(ethylene oxide) by the salt concentration at maximum viscosity indicated that at that point there was binding of one cation per 10 monomer units. Similar results were found by Lundberg, Bailey, and Callard.

In order to be able to evaluate qualitatively the role of anion shielding, the measurements were repeated in the presence of varying amounts of the crown ether dicyclohexyl-18-crown-6. Since cation binding to crown ethers is very much stronger than to poly(ethylene oxide) (see Conductance section), the free cation concentration could be conveniently varied while keeping the anion concentration constant. The resulting plot is also shown in Figure 4. The maximum was decreased and displaced from $\eta = 1.007$ at 2.5×10^{-3} M KBr with no crown ether to $\eta = 0.732$ at 4.6×10^{-3} M KBr with crown ether. The value of 837 sec at 0.0 M free K^+ where $[KBr] = [CE]$ was exactly the same value obtained with the solution of PEO in methanol with no KBr added.

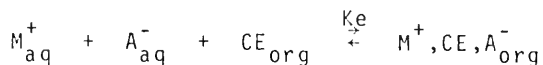
The contribution of the bromide anion in these binding phenomena was further examined by studying the addition of 2.0×10^{-3} M tetramethylammonium bromide to 2.5×10^{-2} M in monomer poly(ethylene oxide) in methanol. The large tetramethylammonium cation should not bind to the polymer to a measurable extent.⁵³ The difference between the viscosity of the poly(ethylene oxide) solution in methanol and that of poly(ethylene oxide) plus tetramethylammonium bromide in methanol was negligible. This indicated that bromide ions did not bind to poly(ethylene oxide) as had been previously proposed.

Light scattering studies have also been done elsewhere on these systems. These measurements confirmed the expansion of poly(ethylene oxide) upon addition of alkali cation salts in the 1.0×10^{-3} to 5.0×10^{-3} M range.⁵⁸

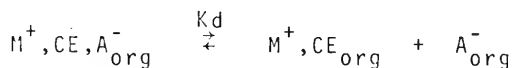
Extraction Equilibria

As stated previously, crown ether complexes of alkali cation salts have been shown to be quite soluble in certain organic solvents. This provided a method for extracting salts from aqueous solutions into organic solvents containing cyclic ethers. Extraction has been efficient only if the anion is large and highly polarizable, as for instance picrate, which has the additional advantage of absorption near 360 nm for easy determination

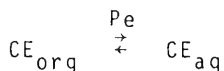
of the amount transferred. The overall equilibrium between an aqueous solution containing alkali cation (M^+), picrate ion (A^-), and hydroxide ion, and an organic solution containing a cyclic polyether (CE) can be described as follows:^{7,59}



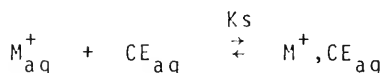
where M^+, CE, A^- designates ion pairs in the organic phase. If the organic phase is polar enough and the concentration of the salt low enough, these ion pairs will dissociate according to



If there is partition of uncomplexed polyether between the two phases, it must be accounted for in another equilibrium.



The final equilibrium takes into account complexation in the aqueous phase if the concentration of crown ether in the aqueous phase is significant.



Due to the solubility of all other polymers in this study in aqueous media, the examination of cation binding by distribution equilibria was limited to poly(acryloyltyrocidine), the polymer containing the antibiotic tyrocidine as a pendant ligand. This process, however, could only be accomplished in a semiquantitative manner. The antibiotic tyrocidine was supplied as a mixture of up to five separate components. Various separation techniques failed to isolate the individual antibiotic units of the mixture. Since the components contain varying amounts of tryptophan and tyrosine amino acid residues, which both absorb at approximately 276 nm in the UV,⁶⁰ and since no other commonly used technique could identify the amounts of the various tyrocidine compounds in the mixture, it was impossible to determine the exact number of antibiotics attached to a polymer chain. It was assumed, therefore, that the antibiotic composition in the polymer was identical with that of the reacting mixture. The UV absorption of the polymeric antibiotic was compared with that of the antibiotic mixture to get an estimate of the number of antibiotic units per polymer. A value of one tyrocidine molecule was found for every 12 monomer units.

The extraction of sodium, potassium, and cesium picrates from an aqueous layer into a chloroform layer containing the polymer was examined due to the ease with which this process could be followed by UV-visible

spectroscopy. The picrate salts were dissolved in water at a concentration of 1.0×10^{-3} M. A large quantity of the corresponding alkali chloride was also added to each aqueous solution to increase the number of alkali ions in the organic layer and also to increase the ionic strength of the aqueous layer which would prevent the chloroform layer from becoming dispersed into the water layer. Poly(acryloyltyrocidine) was added to the chloroform layer at an estimated concentration of 1.3×10^{-4} M in antibiotic units. The amount of salt extracted is presented as a percent of the tyrocidine units present in the organic phase. The results are shown in Table 1. The sodium selectivity of the polymer was similar to the 4:1 sodium over potassium selectivity demonstrated by the antibiotic itself in cation transport through lipid membranes.⁴⁹

Table 1. Extraction of Alkali Picrates from Aqueous Layer into Chloroform Layer Containing Poly(acryloyltyrocidine) at 25°

Cation	Initial Aqueous Layer		Initial Chloroform Layer	Final Chloroform Layer
	[Picrate]	[Chloride]	Approx. [Tyrocidine]	% Extraction
Na	1.0×10^{-3}	5.0×10^{-2}	1.3×10^{-3}	15
K	1.0×10^{-3}	5.0×10^{-2}	1.3×10^{-3}	2
Cs	1.0×10^{-3}	5.0×10^{-2}	1.3×10^{-3}	-

Potentiometry

The use of cation-selective electrodes to determine the stability constants of complexes of crown ethers with various univalent cations has proven to be an effective method with systems having stability constants ranging over six or more orders of magnitude.⁶ The electrodes responded to uncomplexed ions in solution; therefore, after the addition of a ligand, the drop in the potential of the solution directly corresponded to the number of complexed ions. In order to verify the experimental procedures used in this study, binding constants were determined initially for two typical crown ethers and the results were compared to literature values. These data shown in Table 2.

Table 2. Logarithms of Stability Constants of Crown Ethers Added to NaCl in Methanol

Crown Ether	Experimental Binding Constant	Literature Binding Constant
Dicyclohexyl-18-crown-6	3.95 (mixture of isomers)	Isomer A = 4.08 Isomer B = 3.68
18-crown-6	3.89	4.32

The data shown in Table 2 indicate our system gave binding constants close to published values.

Potentiometry was then used to determine the cation binding ability of the antibiotic itself. However, with this system the addition of antibiotic to a salt solution in methanol produced an increase in solution potential instead of the expected decrease. It has been demonstrated that cation-sensitive glass electrodes respond to the presence of various amino acids;⁶¹ therefore, the measured increase in voltage may have been the result of electrode response to the antibiotic itself. As a result, potentiometry was discontinued with this system.

The binding of potassium cations to poly(ethylene oxide) in methanol was a system which could be studied by potentiometry. After addition of the polymer to a potassium chloride solution in methanol, the solution potential dropped corresponding to the binding of potassium ions to the polymer. The new potential was compared to a calibration curve to determine the concentration of remaining unbound cations. From this number, the number of bound cations was calculated and since the number of poly(ethylene oxide) monomer units was known, the number of monomer units per complexed potassium ion could be determined. The data are given in Table 3. As the concentration of poly(ethylene oxide) increased, the number of monomer units per cation increased. This indicated a redistribution of charges along the polymer chains resulting in fewer cations bound per polymer. These ratios of monomer

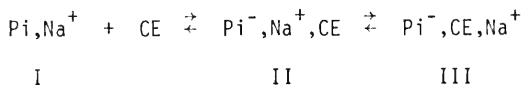
Table 3. Binding of 1.0×10^{-3} M KCl by PEO (molecular weight 100,000) in Methanol at 25°

PEO in Monomer	mV	Uncomplexed K^+	Complexed K^+	Monomer/ K^+
-	36.9	1.0×10^{-3}	-	-
1.14×10^{-2}	28.8	6.1×10^{-4}	3.9×10^{-4}	29
1.83×10^{-2}	23.4	4.3×10^{-4}	5.7×10^{-4}	32
2.39×10^{-2}	17.1	2.7×10^{-4}	7.3×10^{-4}	33
2.96×10^{-2}	9.8	1.3×10^{-4}	8.7×10^{-4}	34
3.30×10^{-2}	7.4	9.1×10^{-5}	9.1×10^{-4}	36
3.44×10^{-2}	6.6	8.2×10^{-5}	9.2×10^{-4}	37
3.58×10^{-2}	6.1	7.2×10^{-5}	9.3×10^{-4}	38
3.87×10^{-2}	5.0	6.0×10^{-5}	9.4×10^{-4}	41
4.00×10^{-2}	4.5	5.2×10^{-5}	9.5×10^{-4}	42
4.14×10^{-2}	3.0	3.0×10^{-5}	9.7×10^{-4}	43

units per cation differ from the value of 10 calculated from conductance studies. These factors will be discussed later.

UV-visible Spectrometry

It has been observed that salts of picric acid in low polarity media frequently exhibited pronounced shifts in their optical spectra upon complexation of the cation by crown ethers.¹⁷ These shifts were most likely due to a significant increase in the interionic distance of the tight ion pair as a result of external coordination of the cation. Further addition of a sufficiently strong complexing ether led to the formation of solvent-separated ion pairs. This process may be described by the following equation:



Complex I is a tight ion pair which upon coordination by crown ether becomes the tight ion pair II which has a slight increase in interionic distance. Further crown ether addition leads to the loose ion pair III. Examples of these species are described in Table 4.¹⁷

The absorption maxima of the sodium and potassium salts in THF are those of contact or tight ion pairs.

Table 4. Absorption Maxima of Picrate Salts in Chloroform in the Presence of Excess Crown Ethers

Salt	Crown	λ_{\max} (nm)	Type Complex
Na ⁺	-	351 ^a	I
	15-crown-5	356	II
	18-crown-6	362	II
K ⁺	-	357 ^a	I
	15-crown-5	378	III
	18-crown-6	365	II

^aThese values refer to tetrahydrofuran solutions of these salts.

The same species would be expected in chloroform if the solubility of the salts were high enough because of the relatively low cation solvating power of this solvent.¹⁷

The presence of 15-crown-5 in chloroform solubilized the sodium salt in the form of a crown-complexed tight ion pair (λ_{\max} 356 nm), resulting in a small increase in the interionic distance. Addition of a large excess of 15-crown-5 to the potassium salt converted this species to a loose ion pair (λ_{\max} 378 nm) which existed as a 2:1 complex. With 18-crown-6, both salts formed tight ion pairs (λ_{\max} 362 to 365 nm) with the interionic distance slightly larger than with the 15-crown-5 sodium complex.

In order to examine the various solvation processes involved when a typical ether ligand is added to sodium picrate in chloroform, a solution of 1.0×10^{-4} M sodium picrate in 10% THF/90% CHCl_3 was titrated with bis [2-(2-methoxy)ethyl]ether or tetraglyme. The small amount of THF aided the solubility of sodium picrate in chloroform but had no effect on the absorption maximum. The results of these additions are plotted in Figure 5. As the concentration of tetraglyme increased, the absorption maximum shifted to longer wavelengths indicating small increases in the interionic distance of the tight ion pair. An analogue of the Benesi-Hildebrande equation for optical absorption allows the calculation of a binding constant from these shifts in the absorption maximum.⁶² The change in absorption on tetraglyme addition from the λ_{max} of sodium picrate without tetraglyme, Δ , can be related to the total tetraglyme concentration [TG] and the binding constant K by the equation

$$\frac{1}{\Delta} = \frac{1}{K} \cdot \frac{1}{\Delta_0} \cdot \frac{1}{[\text{TG}]} + \frac{1}{\Delta_0}$$

A plot of $1/\Delta$ against $1/[\text{TG}]$ should be linear with the intercept at the ordinate yielding Δ_0 and the gradient yielding the product $K\Delta_0$. Dividing this product by Δ_0 yields the binding constant K. Benesi-Hildebrande plots for the addition of tetraglyme to sodium picrate in

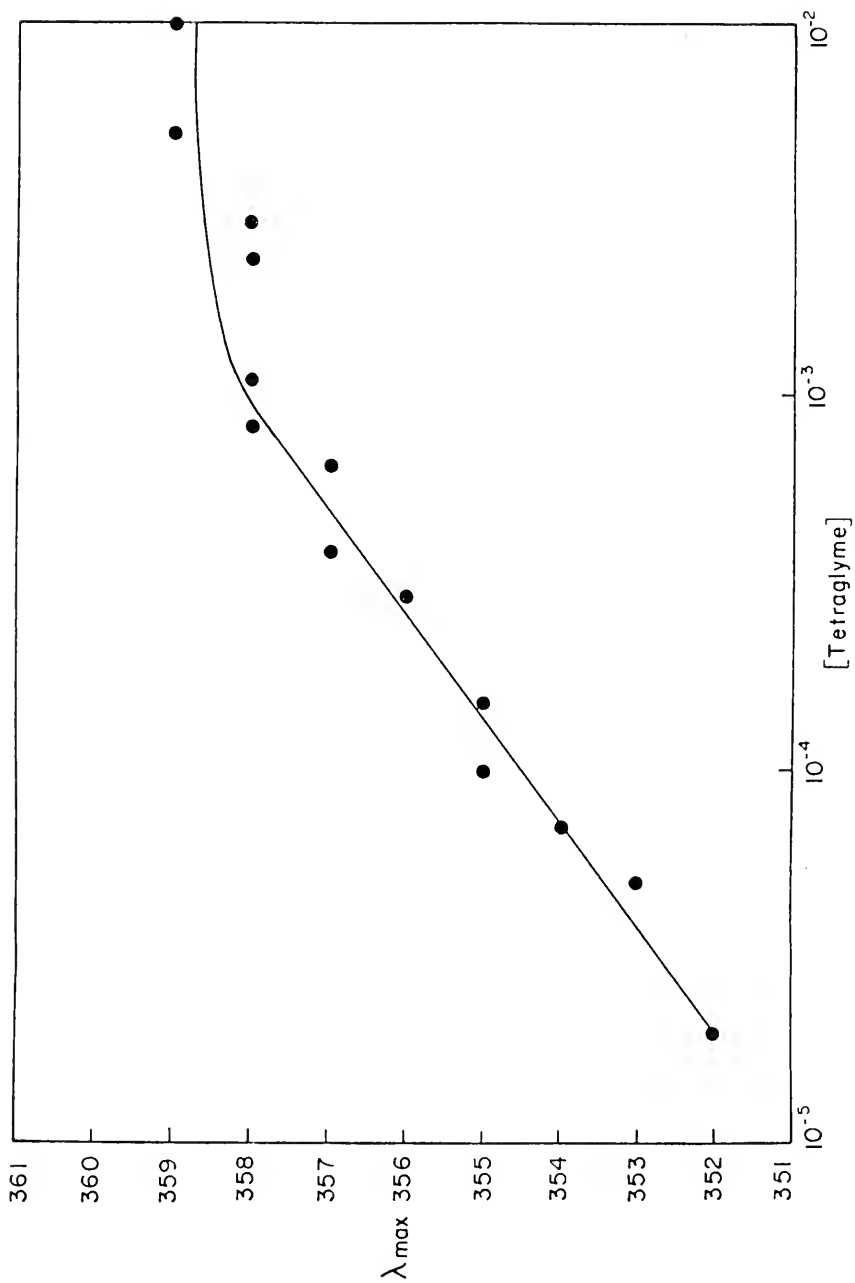


Figure 5. Absorption Maxima Upon Addition of Tetraglyme to Sodium Picrate at 25°

10% THF/90% CHCl_3 are given in Figure 6 and Figure 7. Results of these plots are given in Table 5. Over the entire concentration range examined, the Benesi-Hildebrand plots were linear and the binding constants were consistent. This is the first instance where shifts in the picrate spectra due to added ligand have been used to calculate a binding constant.

In the graph of absorption maxima vs. tetraglyme concentration, Figure 5, a gradual increase in interionic distance was observed up to a λ_{max} of 359 nm. It was expected that the addition of ligand to picrate salt could distinguish between the coordinating ability of the various complexing polyethers under analysis. These materials included 1,2-dimethoxyethane, bis(2-methoxyethyl)ether or diglyme, tetraglyme, poly(ethylene oxide) of various molecular weights, and the polymeric vinyl glyme poly(3,6,9,12,15-pentaoxa-1-heptadecene). The results of the addition of 1.0×10^{-3} M and 1.0×10^{-4} M ligand (in monomer units) to 1.0×10^{-4} M sodium picrate are given in Table 6. With the exception of DME and diglyme, there was very little difference between the coordinating ability of the various complexing polyethers.

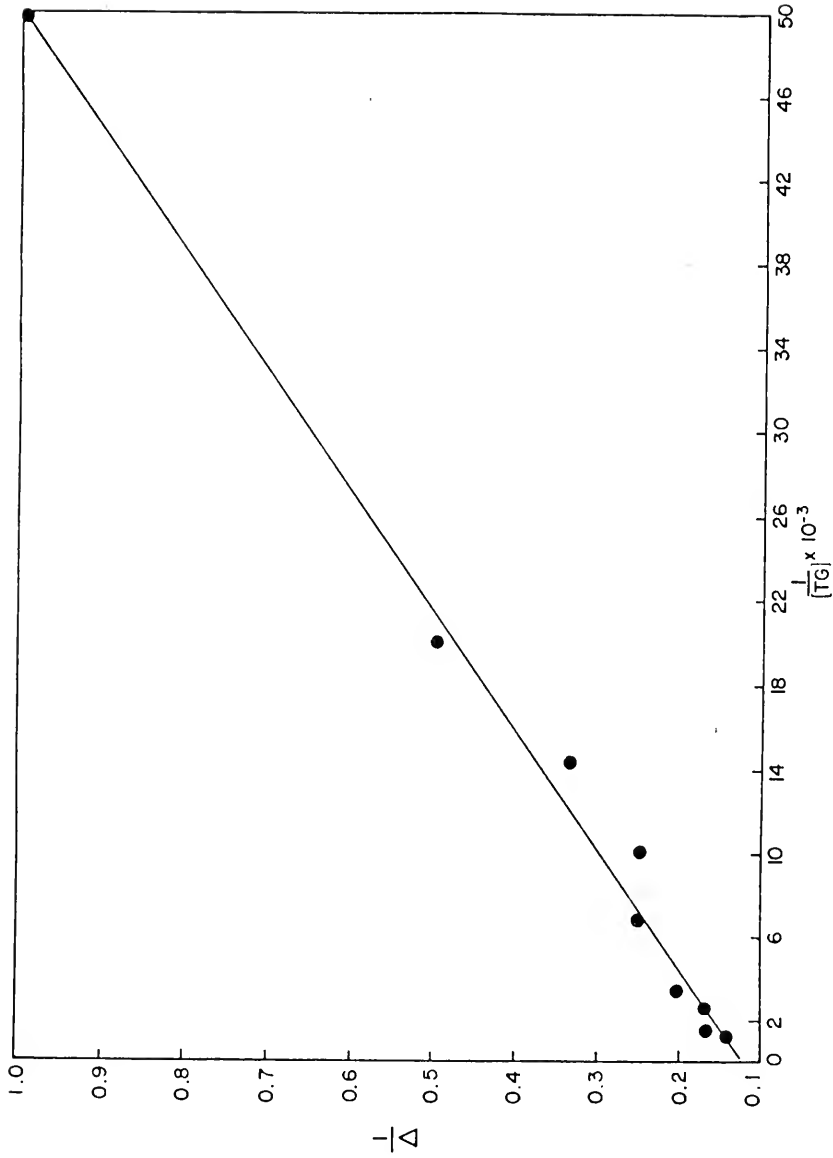


Figure 6. Benesi-Hildebrand Plot for Initial Tetraglyme Additions to NaBPh_4 at 25°

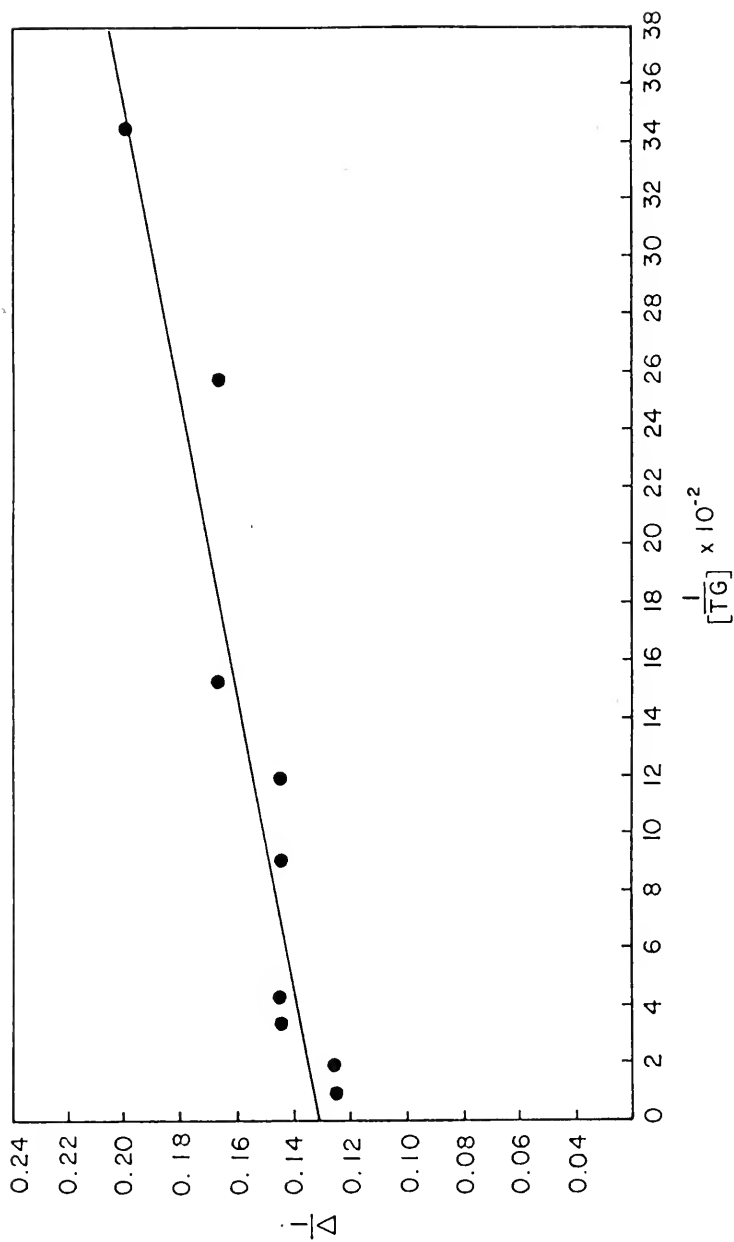


Figure 7. Benesi-Hildebrand Plot for Large Tetraglyme Additions to NaBPh_4 at 25°

Table 5. Binding Constant of Tetraglyme Addition to 1.0×10^{-4} M Sodium Picrate in 10% THF/90% CHCl_3 from Benesi-Hildebrande Plots

Tetraglyme Range	Intercept ($\frac{1}{\Delta_0}$)	Slope ($\frac{1}{K} \cdot \frac{1}{\Delta_0}$)	K ($l \cdot M^{-1}$)
2.0×10^{-5} M - 8.3×10^{-4} M	1.20×10^{-1}	1.76×10^{-5}	6.8×10^3
2.9×10^{-4} M - 1.0×10^{-2} M	1.31×10^{-1}	2.00×10^{-5}	6.5×10^3

Table 6. Absorption Maxima After Addition of Ethers of Various Molecular Weights to 1.0×10^{-4} M Sodium Picrate in 10% THF/90% CHCl_3

Ether	Mol. Wt.	1.0×10^{-4} M Ether max (nm)	1.0×10^{-3} M Ether max (nm)
DME	90	351	352
Diglyme	134	351	352
Tetraglyme	222	355	358
PEO	600	353	358
PEO	1000	353	359
PEO	4000	352	357
PEO	6000	352	357
PEO	100,000	352	357
PEO	300,000	352	357
PEO	900,000	352	357
P(PHD)	40,000	353	357

Conductance

Pedersen and Frensdorff obtained information on the stoichiometry of crown ether-alkali cation complexes by measuring conductance of salt solutions after addition of crown ethers.⁵⁹ When the polarity of the solvent was high enough and the salt concentration low enough to ensure complete dissociation of the ions, the mobility of the cation decreased as it became complexed to the crown ether resulting in a decreased conductance of the salt solution.

Where the binding constant, K , defined by



was high, the conductance decreased linearly with an increase in [crown ether] until complexation is virtually complete. Further addition of crown ether had no effect. Such plots are shown in Figures 8 and 9. Here it is demonstrated that a break in the curve occurs at a crown to salt ratio equal to the stoichiometry of the complex. Smid has also shown that addition of a poly(vinyl crown ether) to a salt solution reduced the conductance more than the corresponding monomeric crown ether because of the lower mobility of the polymeric complex.⁴³ Significantly in the polymer case, the equivalent conductance decreased somewhat beyond the

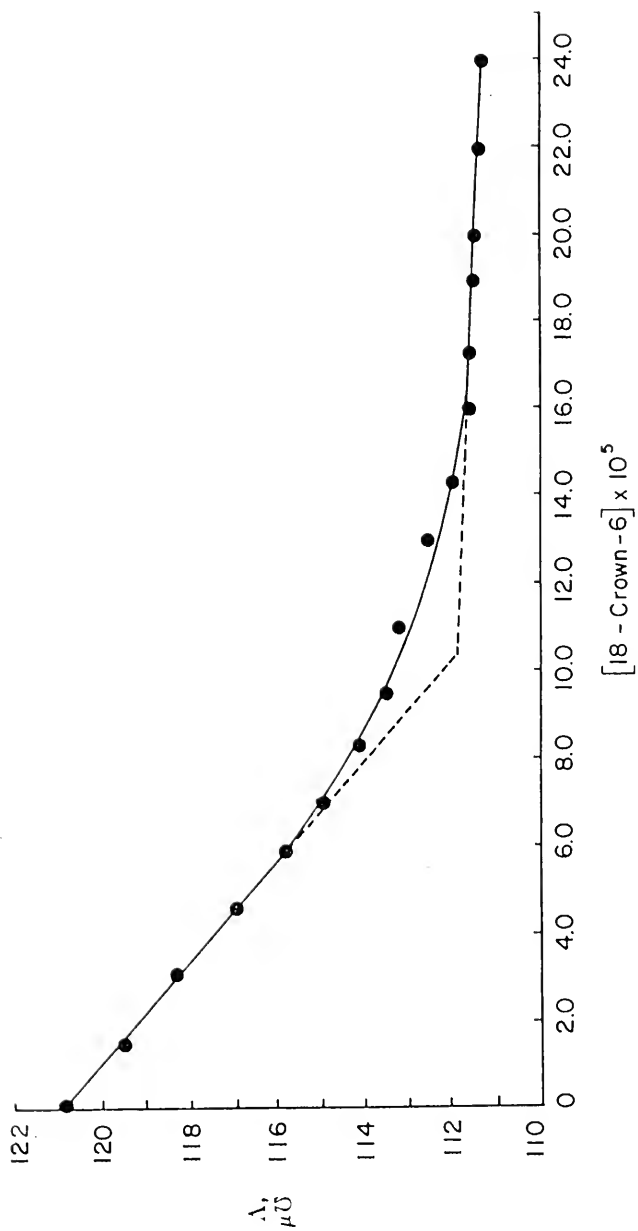


Figure 8. Conductance of 1.0×10^{-4} M NaBPh_4 + 18-crown-6 in CH_3CN at 25°

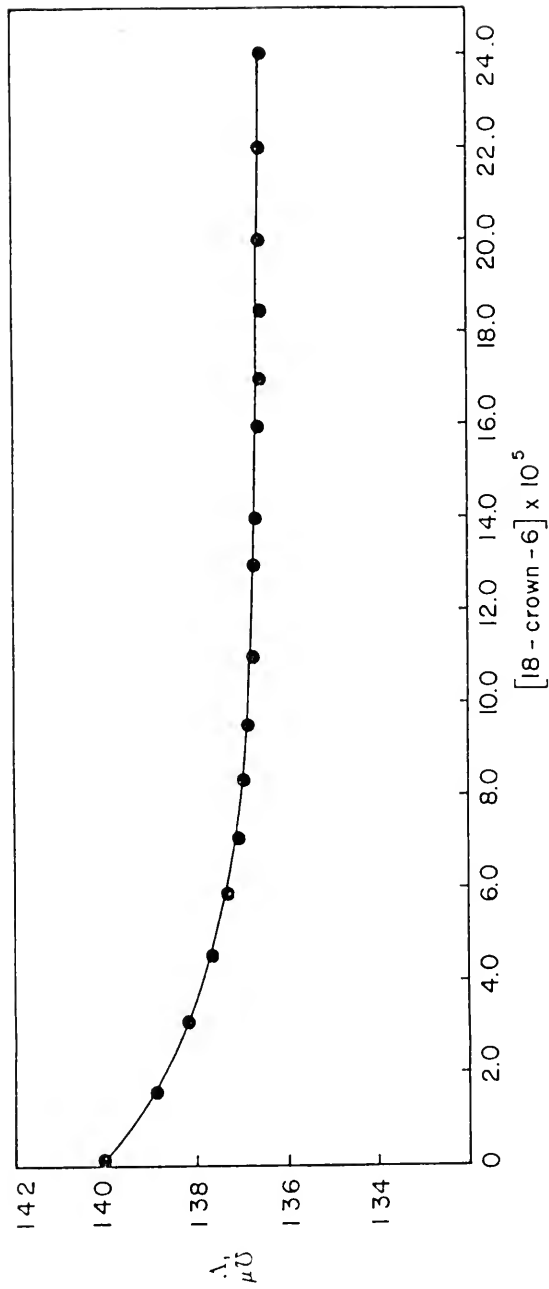


Figure 9. Conductance of 1.0×10^{-4} M NaBPh₄ + 18-crown-6 in Acetone at 25°

stoichiometric crown ether to cation ratio. This gradual decrease beyond the break point is probably due to redistribution of cations upon addition of more polymer,⁴² a point which will be discussed later.

Several studies were performed on various molecular weights of poly(ethylene oxide) and on poly(pentaoxa-1-heptadecene), or P(PHD), in order to investigate some of the factors involved in conductance measurements. There are several complicating factors which can influence conductance determinations: (1) Viscosity effects on ion mobility could be a problem especially with polymers. As polymers are added to a salt solution, the viscosity of the medium may increase to the point where mobility of the ions is decreased. This would result in a drop in conductance without cations being bound to the polymer. The relationship between conductance and viscosity of a solution is given by Walden's Rule:⁶³

$$\lambda_0 \eta = \text{constant}$$

This rule states that the product of limiting equivalent conductance, λ_0 , and macroscopic viscosity, η , of a system is equal to a constant. In order for the product to remain a constant, an increase in macroscopic viscosity requires a corresponding decrease in λ_0 . (2) It is also possible for the anion of the salt to effect the conductance if it were complexed by the polymer. In this case, a drop in

conductance of a salt solution upon addition of a polymer would indicate a decrease in anion mobility as well as cation mobility. (3) Another possible problem is polymer conductance. If the polymer itself conducts, the conductance measured upon polymer addition would be higher than the true value.

In order to examine the possible effects of macroscopic viscosity on conductance, a polymer was needed which does not complex cations. This polymer could then be added to a salt solution with any resulting decrease in conductance being attributed to an increase in viscosity. The polymer chosen was poly(styrene). The solvent was THF due to the solubility of poly(styrene) in this solvent and the fact that NaBPh_4 exists as free ions in THF at low concentrations.⁶⁴ The addition of poly(styrene) up to 4.0×10^{-2} M in monomer to 1.0×10^{-5} M NaBPh_4 caused virtually no change in conductance. Since viscosity studies demonstrated a 20% increase in macroscopic viscosity for this polymer concentration, it can be concluded from Walden's Rule that this increase in macroscopic viscosity due to the addition of polymer in this low concentration range was of no consequence in the conductance measurements.

Another method used for determining the effects of macroscopic viscosity on conductance was adding polymer to a solution of tetrabutylammonium tetraphenylboride.

Since the tetrabutylammonium cation does not bind to polyethers (see Viscosity section), any decrease in conductance should be attributable to the lowering of ion mobilities due to an increase in macroscopic viscosity. The conductance measured upon binding of alkali cations to the polymers could then be corrected by this value. Poly(pentaoxa-1-heptadecene) was added over a concentration range of 3.2×10^{-3} - 4.0×10^{-2} M in monomer to a 1.0×10^{-4} M solution of tetrabutylammonium tetraphenylboride in THF. No significant change in conductance was measured over this concentration range of polymer. These results were consistent with the various poly(ethylene oxides) studied in this concentration range. For higher polymer concentrations, however, significant viscosity effects were measured. Some examples of the viscosity studies are shown in Table 7.

The lack of conductance decrease on addition of low concentrations of poly(ethylene oxide) to tetrabutylammonium tetraphenylboride also indicated the lack of anion binding. Any anion binding would have resulted in a measurable decrease in conductance over the polymer concentration range of 3.2×10^{-3} to 4.0×10^{-2} M in monomer.

The conductance of the polymers themselves was measured by adding the polymer to pure solvent. These values could then be subtracted from the measured

Table 7. Decrease in Conductance Due to Polymer Viscosity at 25°

Polymer	[Monomer]	Salt	Concentration, M	Solvent	Maximum Change in Conductance, Δ in $\mu\Omega$
Poly(styrene)	3.2×10^{-3} - 4.0×10^{-2}	NaBPh ₄	1.0×10^{-5}	THF	-
P(PHD)	3.2×10^{-3} - 4.0×10^{-2}	Bu ₄ NBPh ₄	1.0×10^{-4}	THF	-
P(PHD)	1.1×10^{-3} - 1.0×10^{-1}	Bu ₄ NBPh ₄	1.0×10^{-4}	CH ₃ CN	2.20
PEO 1000	1.1×10^{-3} - 1.0×10^{-1}	Bu ₄ NBPh ₄	1.0×10^{-4}	CH ₃ CN	3.60
PEO 6000	1.1×10^{-3} - 1.0×10^{-1}	Bu ₄ NBPh ₄	1.0×10^{-4}	CH ₃ CN	5.16

conductance of the polymer-salt solutions. Examples of the conductance of several polymers are given in Table 8.

Table 8. Conductance of Polymers in CH_3CN at 25°

Polymer	Molecular Weight	[Monomer]	Polymer Conductance, Λ , in $\mu\Omega$
PEO	1,000	5.0×10^{-3}	1.30
		1.0×10^{-1}	18.90
PEO	6,000	5.0×10^{-3}	-
		1.0×10^{-1}	-
PEO	100,000	5.0×10^{-3}	0.10
		1.0×10^{-1}	2.10
PEO	900,000	5.0×10^{-3}	0.10
		1.0×10^{-1}	3.00
P(PHD)	40,000	5.0×10^{-3}	1.30
		1.0×10^{-1}	22.70

An example of the effect of polymer addition to a salt solution is shown in Figure 12. It may be contrasted with the conductance plot obtained by addition of 18-crown-6, a strong cation complexing agent of low molecular weight, to a similar salt solution in Figure 8. Both figures are characterized by two separate sections.

Initially there is a region of sharply decreasing conductance in which cation binding takes place. A comparison of initial slopes indicates that the crown ether curve is much steeper in this region than the polymer. Further addition of ligand causes a gradual decrease in both slopes. This was also found with all other polymer systems studied. The second portion of the crown ether figure is a nearly horizontal line indicating that all cations have been bound and that further crown ether addition has no effect on conductance. The second segment of the polymer curve, however, continues to decrease in conductance upon addition of more polymer. This is due to a redistribution of cations among the polymer chains. All the polymers examined except PEO 1000 gave this conductance decrease with cation redistribution. The results of the conductance studies are given in Table 9.

Solvent effects. The effects of various solvents on the complexation process were examined by adding P(PHD) over a concentration range of 3.2×10^{-3} to 1.0×10^{-1} M in monomer to 1.0×10^{-4} M NaBPh_4 in acetone, tetrahydrofuran, and acetonitrile. These additions were made over two concentration ranges: from 3.2×10^{-4} M to 4.8×10^{-3} M and from 5.0×10^{-3} M to 1.0×10^{-1} M in monomer. Examples of these results are given in Figures 10-15. The results are given in Table 10.

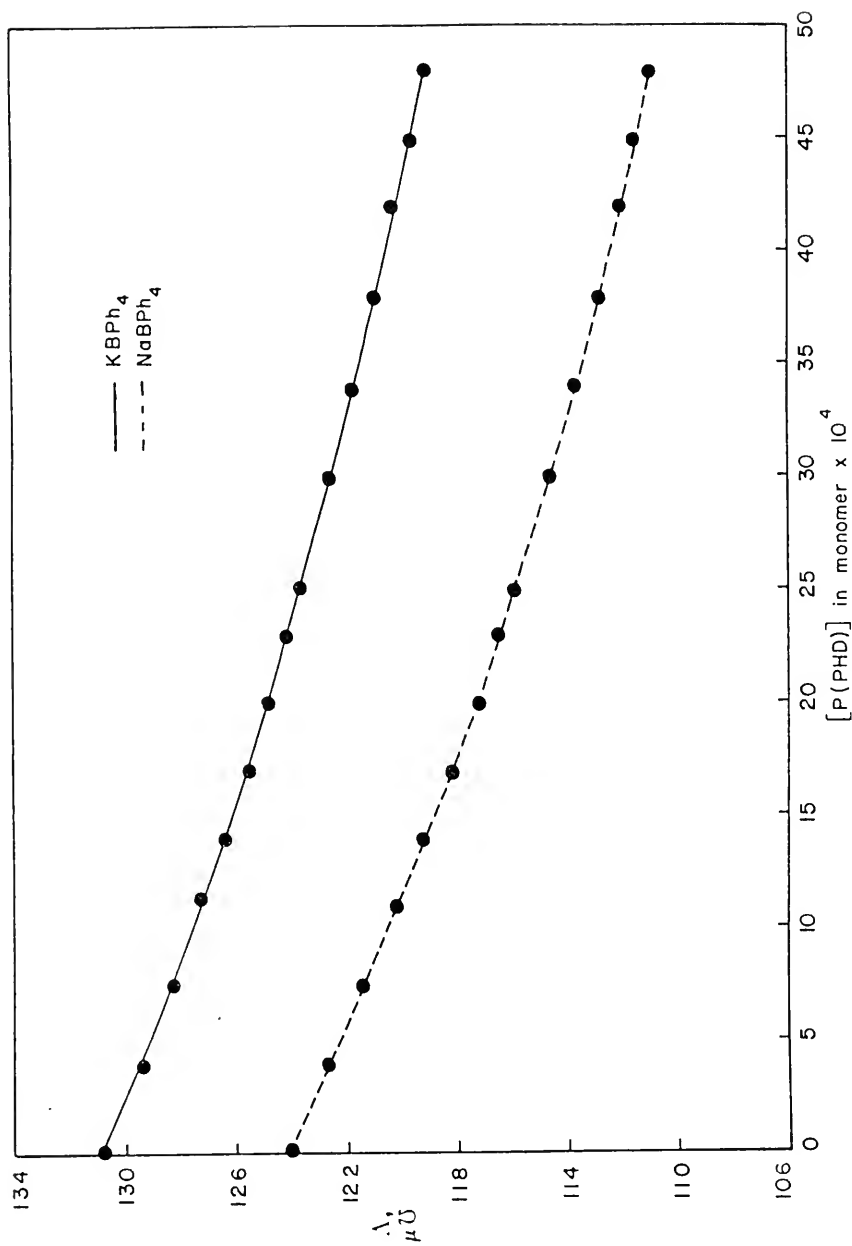


Figure 10. Conductance of 1.0×10^{-4} M Tetraphenylboride Salts + Low Amounts P(PHD) in CH_3CN at 25°

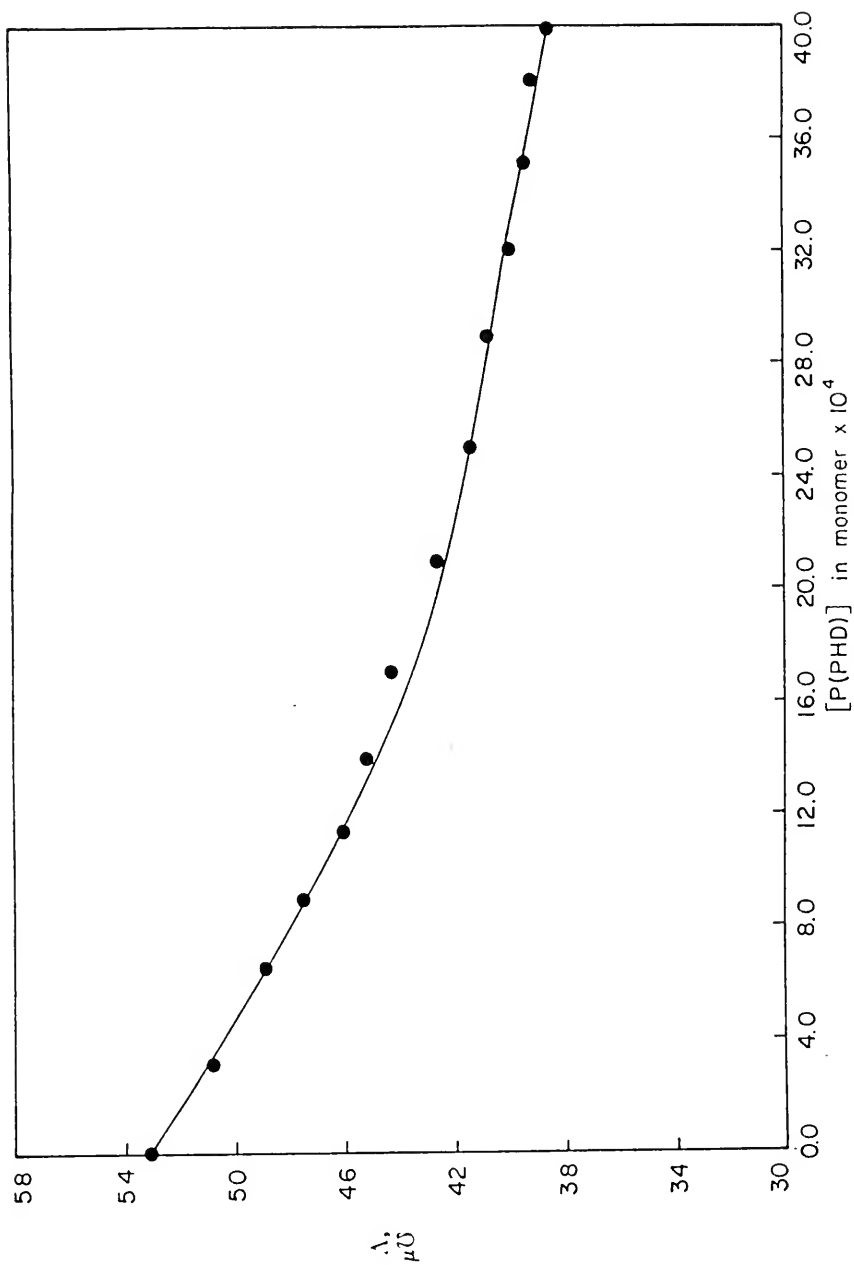


Figure 11. Conductance of 1.0×10^{-4} M NaBPh_4 + Low Amounts P(PHD) in THF at 25°

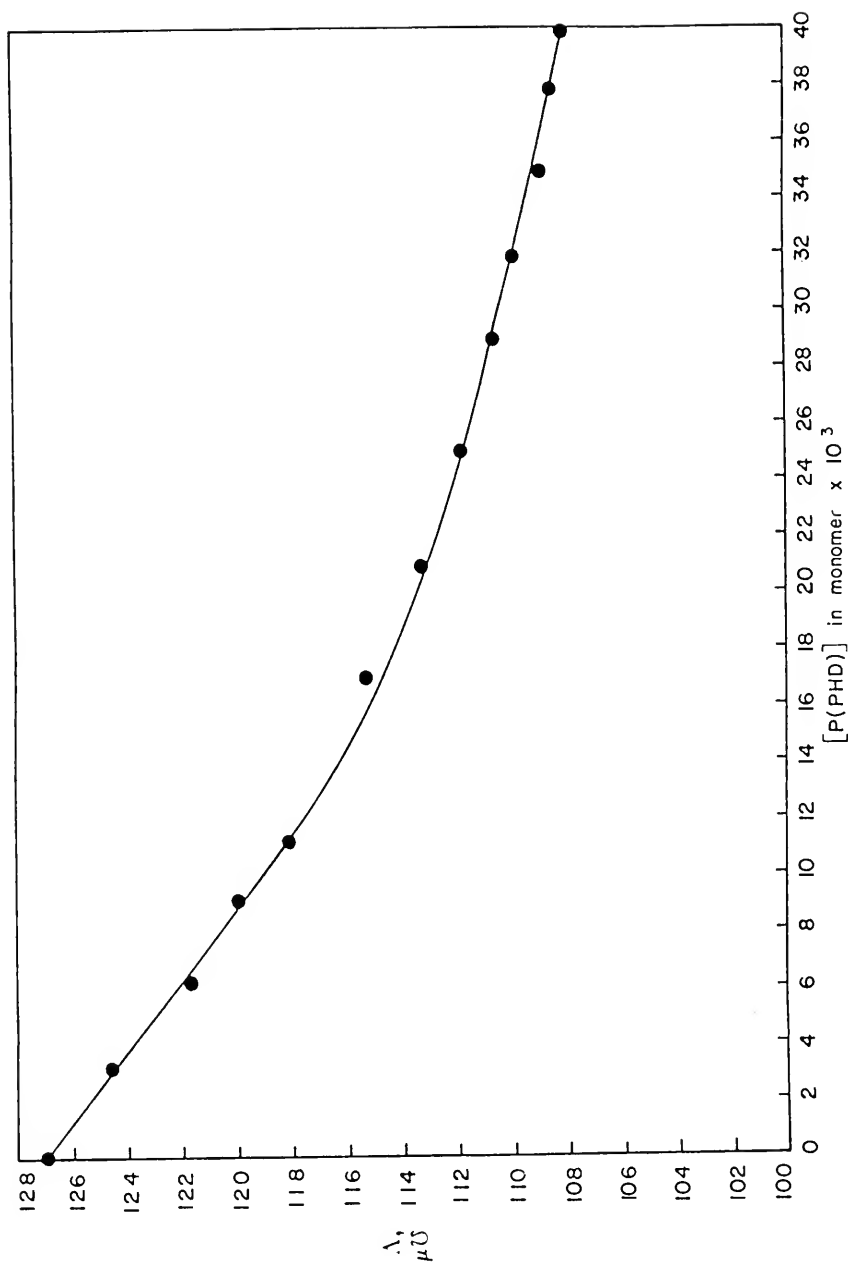


Figure 12. Conductance of 1.0×10^{-4} M NaBPh_4 + Low Amounts P(PHD) in Acetone at 25°

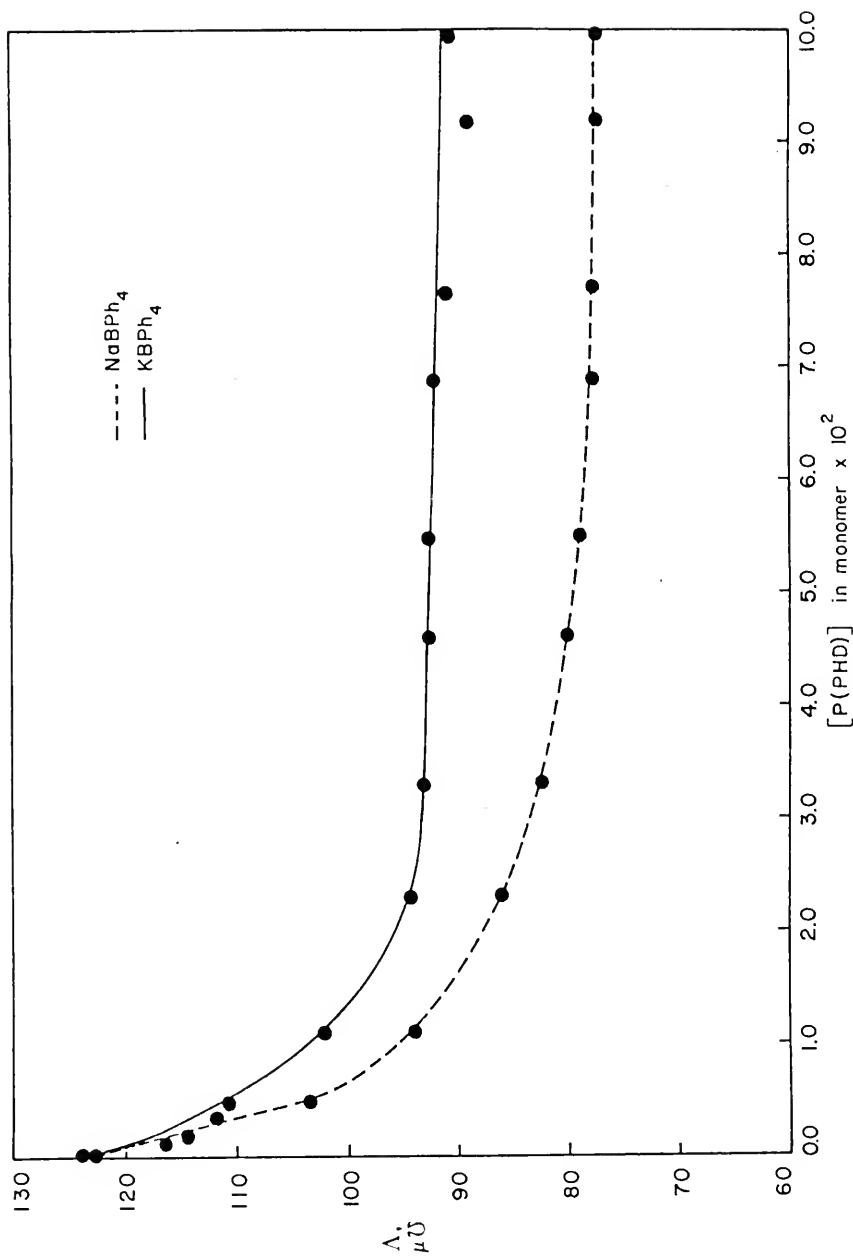


Figure 13. Conductance of 1.0×10^{-4} M Tetraphenylboride Salts + Large Amounts P(PHD) in CH_3CN at 25°

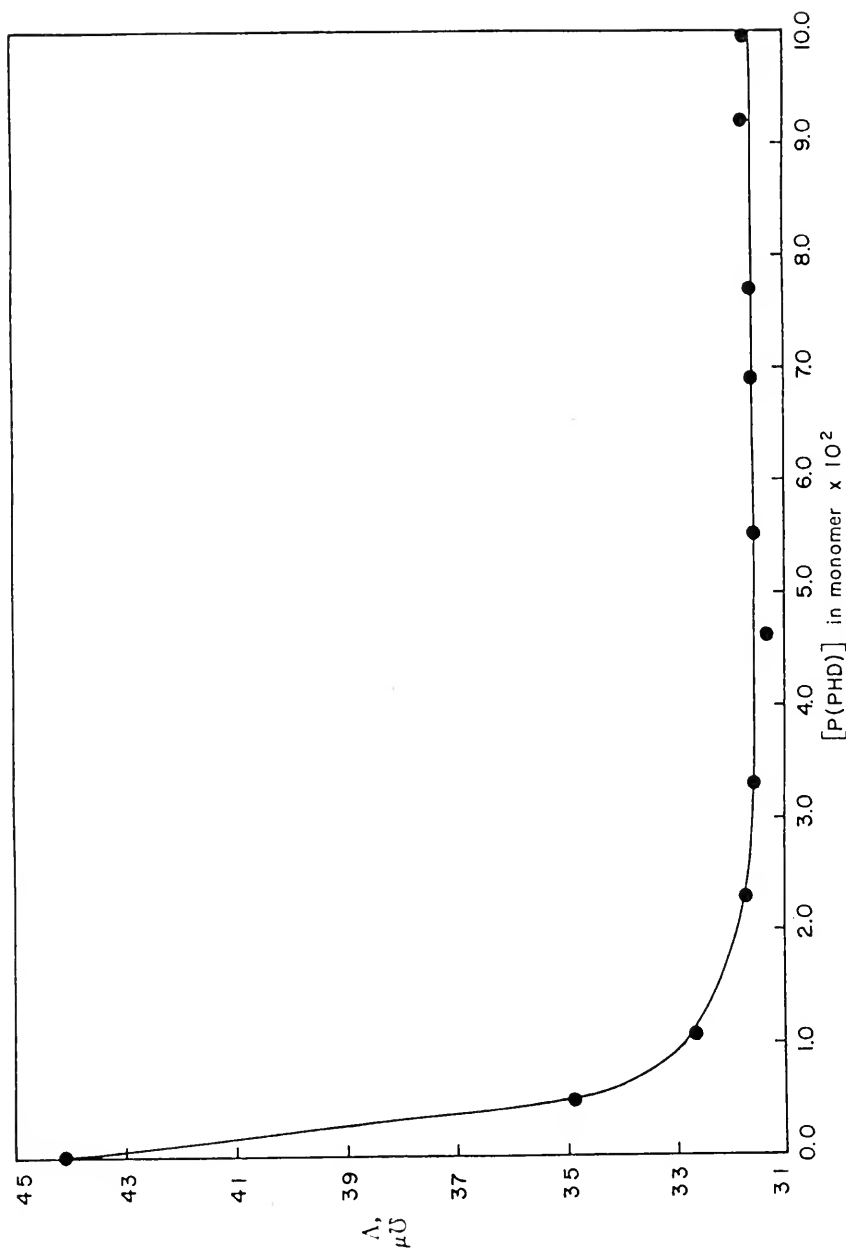


Figure 14. Conductance of 1.0×10^{-4} M NaBPh_4 + $P(PHD)$ in THF at 25°

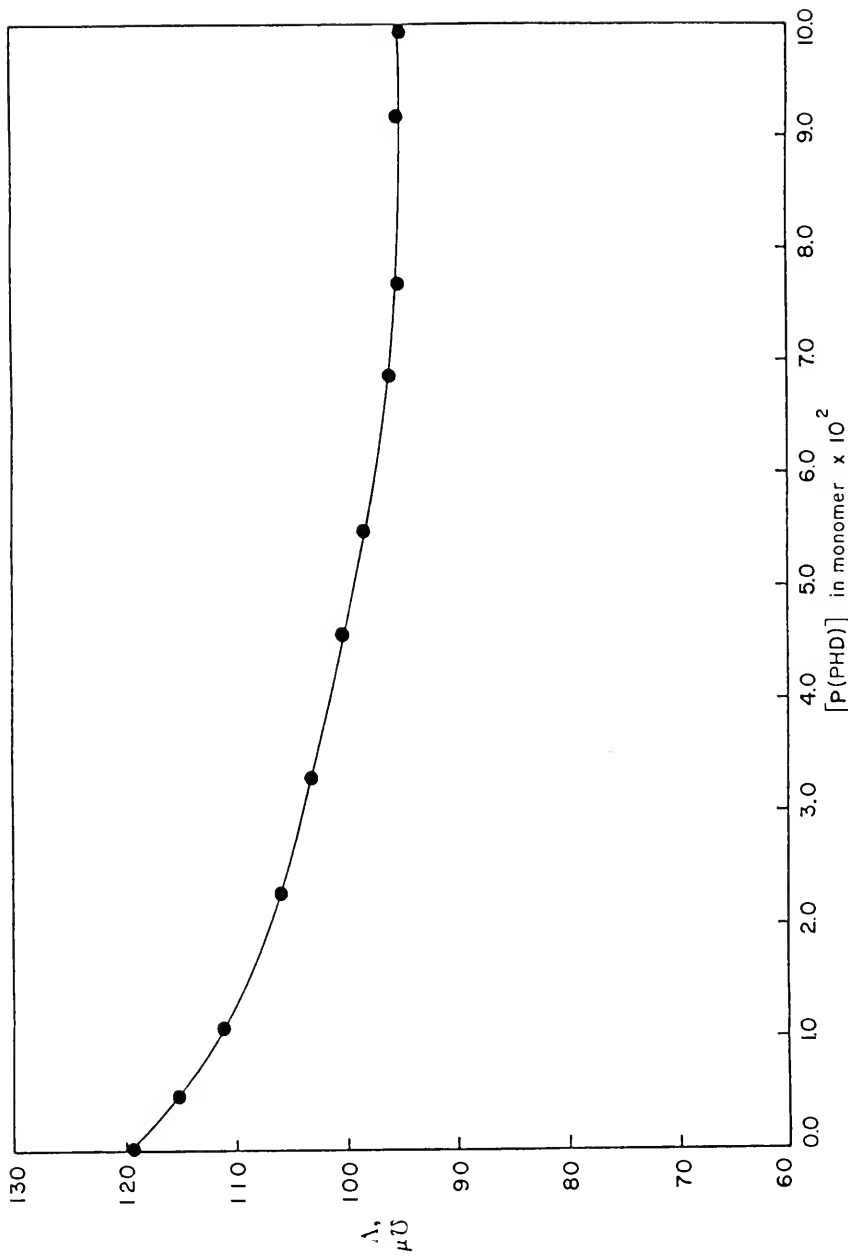


Figure 15. Conductance of 1.0×10^{-4} M NaBPh_4 + P(PHD) in Acetone at 25°

Table 9. Conductance Studies of Polyethers with 1.0×10^{-4} M Tetraphenylboride Salts

Ligand	Ligand Concentration Range (in monomer), M	Salt	Solvent	Initial Slope	[Monomer] at Approx. Point of Complete Binding, μg
Tetraglyme	3.2×10^{-3}	4.0×10^{-2}	3.2×10^{-3}	-	-
P(PHD) ^a	3.2×10^{-3}	4.0×10^{-2}	3.2×10^{-3}	-	-
P(PHD)	5.0×10^{-3}	1.0×10^{-1}	5.0×10^{-3}	-	1.0×10^{-1}
P(PHD)	4.5×10^{-5}	5.6×10^{-4}	4.5×10^{-5}	-	-
P(PHD)	4.5×10^{-4}	5.6×10^{-4}	4.5×10^{-4}	-	-
P(PHD)	3.2×10^{-4}	4.0×10^{-3}	3.2×10^{-4}	-	-
P(PHD)	5.0×10^{-4}	1.0×10^{-1}	5.0×10^{-4}	-	3.3×10^{-2}
P(PHD)	3.9×10^{-3}	4.8×10^{-3}	3.9×10^{-3}	-	-
P(PHD)	1.1×10^{-3}	1.0×10^{-1}	1.1×10^{-3}	-	-
P(PHD)	3.9×10^{-4}	4.8×10^{-3}	3.9×10^{-4}	-	7.5×10^{-2}
P(PHD)	1.1×10^{-3}	1.0×10^{-1}	1.1×10^{-3}	-	-
18-crown-6	1.6×10^{-5}	2.4×10^{-4}	1.6×10^{-5}	-	6.0×10^{-2}
18-crown-6	1.6×10^{-4}	2.4×10^{-4}	1.6×10^{-4}	-	1.8×10^{-4}
PEO 1,000	3.9×10^{-4}	4.8×10^{-3}	3.9×10^{-4}	-	1.6×10^{-4}
PEO 1,000	1.1×10^{-3}	1.0×10^{-1}	1.1×10^{-3}	-	-
PEO 6,000	3.9×10^{-4}	4.8×10^{-3}	3.9×10^{-4}	-	3.3×10^{-2}
PEO 6,000	1.1×10^{-3}	1.0×10^{-1}	1.1×10^{-3}	-	-
PEO 100,000	3.9×10^{-4}	4.8×10^{-3}	3.9×10^{-4}	-	1.0×10^{-1}
PEO 100,000	1.1×10^{-3}	1.0×10^{-1}	1.1×10^{-3}	-	-
PEO 900,000	3.9×10^{-4}	4.8×10^{-3}	3.9×10^{-4}	-	-
PEO 900,000	1.1×10^{-3}	1.0×10^{-1}	1.1×10^{-3}	-	-

^a Molecular weight 40,000^b 1.0×10^{-5} M salt concentration

Table 10. Solvent Effects on Conductance of P(PHD) Added to 1.0×10^{-4} M NaBPh₄ Solutions

Solvent	Donor Number ⁶⁵	Dipole Moment ⁶⁶	[Polymer] in Monomer	Slope	Apparent Point of Complete Binding, M
Acetone	17.0	2.88	$3.2 \times 10^{-4} - 4.0 \times 10^{-3}$	-7.80×10^2	1.0×10^{-1}
			$5.0 \times 10^{-3} - 1.0 \times 10^{-1}$	-1.20×10^3	
Acetonitrile	14.1	3.92	$3.2 \times 10^{-4} - 4.0 \times 10^{-3}$	-3.35×10^3	7.5×10^{-2}
			$5.0 \times 10^{-3} - 1.0 \times 10^{-1}$	-3.03×10^3	
THF	20.0	1.63	$3.2 \times 10^{-4} - 4.8 \times 10^{-3}$	-6.25×10^3	3.3×10^{-2}
			$5.0 \times 10^{-3} - 1.0 \times 10^{-1}$	-1.85×10^3	

For lower polymer concentration range, THF gave the largest slope followed by acetonitrile and then acetone. For the higher polymer concentration range, the largest slope was found in acetonitrile followed by THF and acetone. The apparent point of complete cation binding is the point at which the conductance curve approaches a horizontal line. Beyond this point, there is very little if any change in conductance upon addition of more polymer. The apparent point of complete binding was reached first in THF followed by acetonitrile and acetone. The competition between solvent and ligand for solvation of sodium cations was also examined by adding 18-crown-6 to NaBPh_4 in acetone and acetonitrile, Figures 8 and 9 and Table 9. As with P(PHD) the highest slope and earliest point of complexation of all cations occurred in acetonitrile. This trend does not follow that expected from comparison of either the Gutmann donor number for the solvents or the dipole moment. The Gutmann donor number of a solvent is a property which expresses the total amount of interaction between the solvent and the Lewis acid SbCl_5 , including contributions both by dipole-dipole or dipole-ion interactions and by the binding effect caused by the availability of the free electron pair, and to some extent even steric properties of the solvent molecules. Thus the donor number is considered a semiquantitative measure of solute-solvent interactions.⁶⁵ A higher donor number

would mean a stronger solvation of a cation. The dipole moment gives an indication of the solvent-cation interactions from strictly ion-dipole considerations.⁶⁶

Cation effects. Comparisons were also made between sodium and potassium ions with P(PHD) in acetonitrile and THF. Salt concentrations of 1.0×10^{-4} M in acetonitrile and 1.0×10^{-5} M in THF ensured the presence of free ions.^{64,67} From Table 9 it may be seen that in both solvents and for both the lower and higher polymer concentration ranges, sodium gave a larger slope than potassium.

Molecular weight effects. In order to determine if there was a relationship between molecular weight and binding as measured by conductance, several polyethers of various molecular weights were added to 1.0×10^{-4} M solutions of NaBPh_4 . The polyethers ranged from tetraglyme with a molecular weight of 222 to several poly(ethylene oxide) samples with molecular weights of 1000, 6000, 100,000, and 900,000. Tetraglyme was added over a concentration range of 3.2×10^{-3} M to 4.0×10^{-2} M to a 1.0×10^{-4} M solution of NaBPh_4 in acetone. The change in conductance was negligible because the mobility of the complexed ion was essentially the same as that of the uncomplexed ion.

The poly(ethylene oxide) samples were added to 1.0×10^{-4} M NaBPh_4 in CH_3CN . As with the P(PHD) samples

mentioned earlier, the additions were made over a low concentration range of 3.9×10^{-4} M to 4.8×10^{-3} M in monomer and a high range of 1.1×10^{-3} M to 1.0×10^{-1} M in monomer. The results of PEO 1000, 6000, and 100,000 are given in Figures 16 and 17. The initial slopes were seen to decrease with molecular weight from -5.21×10^{-3} with PEO 1000, -5.16×10^{-3} with PEO 6000, and -4.19×10^{-3} with PEO 100,000 to only -4.11×10^{-3} with PEO 900,000. However, the final segments of the curves, which began to approach a horizontal line, were found at higher conductance values with the lower molecular weight polymers. At 1.0×10^{-1} M in monomer for each polymer, the conductance values ranged from 86.00 μS for PEO 1000 and 70.84 μS for PEO 6000, to 60.30 μS for PEO 100,000 and 60.60 μS for PEO 900,000. Only PEO 1000 and 6000 gave curves which actually approached a horizontal line at higher polymer concentrations. The point at which the horizontal line was approached came at a lower polymer concentration with PEO 1000. For both PEO 100,000 and 900,000 the conductance continued to decrease at high polymer concentrations. As stated earlier, this decrease was probably due to a redistribution of cations along the polymer chains. This will be discussed later.

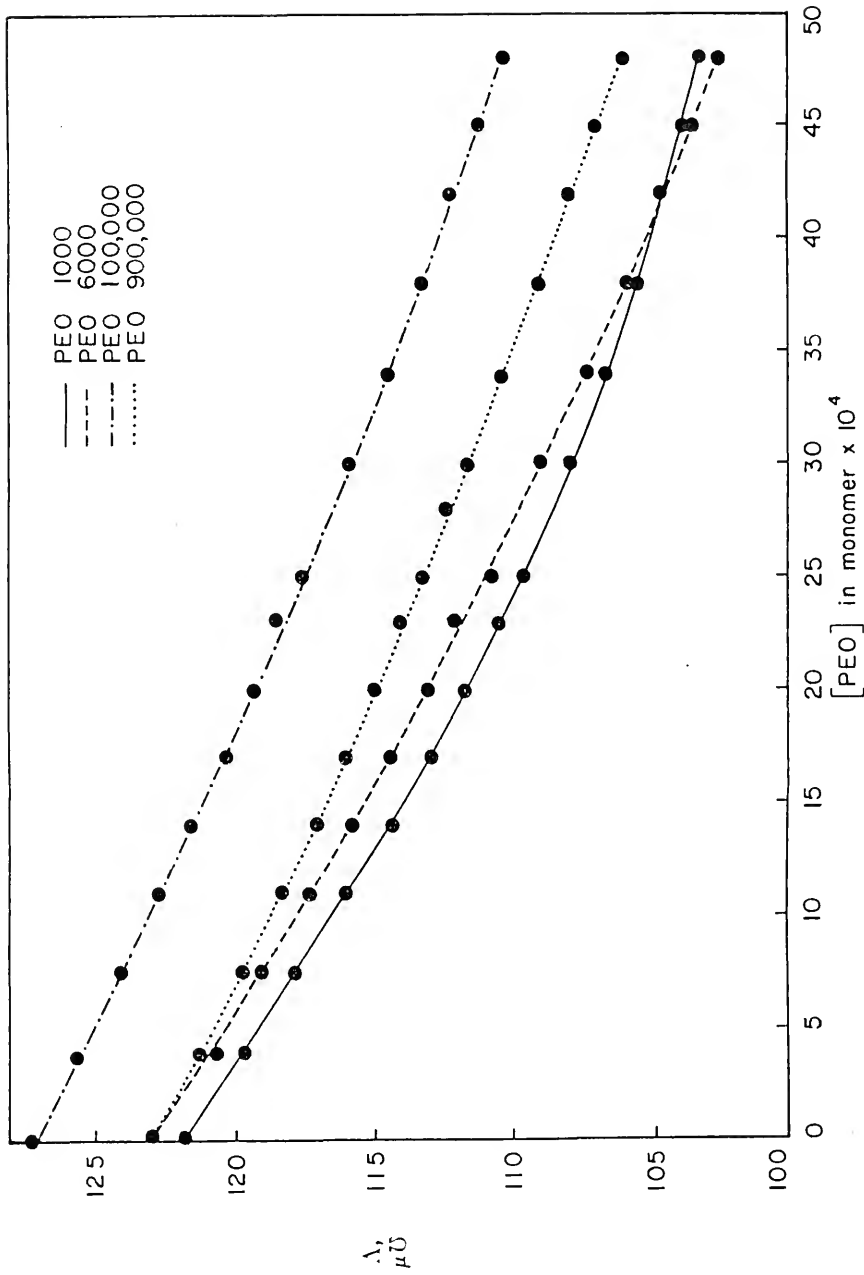


Figure 16. Conductance of 1.0×10^{-4} M NaBPh_4 After Initial PEO Additions in CH_3CN at 25°

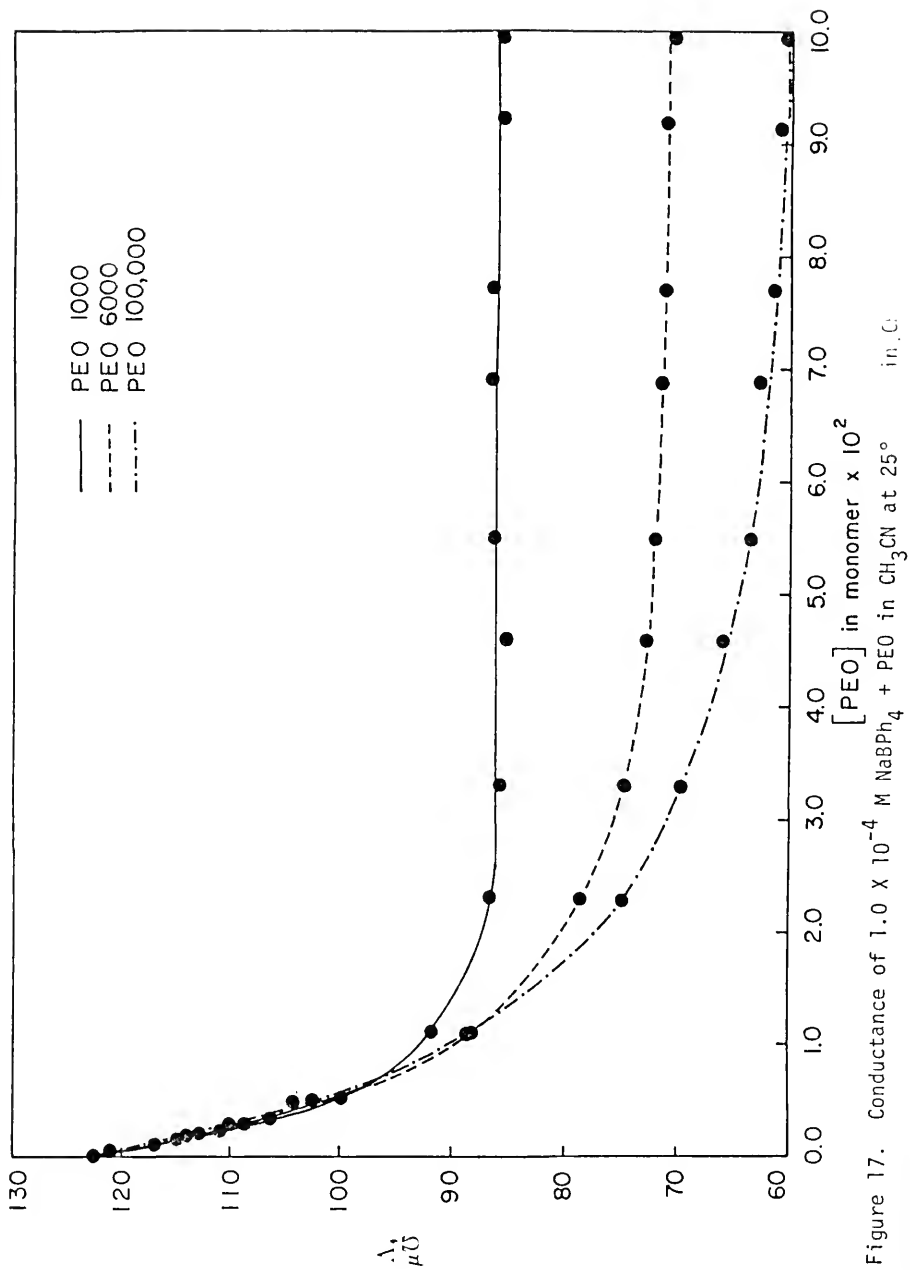
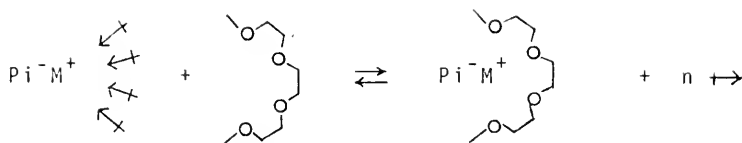


Figure 17. Conductance of 1.0×10^{-4} M NaBPh_4 + PEO in CH_3CN at 25° in $^\circ\text{C}$.

Discussion of Glymes and Poly(ethylene oxides)

UV-visible Spectroscopy

From the spectral data in Table 6, it was determined that the various polyethers in this study coordinate sodium cations. This was evident from the red shifts due to an increase in interionic distance upon addition of ligand. These shifts were almost negligible with DME and diglyme even at higher ether concentration, but with tetraglyme and the polymeric ethers larger red shifts were observed. The absence of distinct red shifts with DME and diglyme indicated that these ethers have very low binding constants with sodium picrate in the low polarity THF/ CHCl_3 solvent. When the shifts with tetraglyme and the polymeric ethers were compared with the changes in λ_{max} upon addition of crown ethers, Table 4, it was apparent that 1.0×10^{-4} M sodium picrate in the presence of 1.0×10^{-3} M glymes, PEO, and P(PHD) remained as a peripherally solvated tight ion pair absorbing at approximately 358 nm (see Results).⁶⁸ In the peripherally solvated ion pair, the ligands are able to replace most of the solvent molecules from the anion paired cation, but coordination is not sufficiently strong to cause a large increase in interionic distance as with crown ethers. This coordination may be represented as follows.



Here solvent molecules, $\times \rightarrow$, are replaced in the cation solvation sphere by ether oxygens of a polyether. From an entropy standpoint, the coordination would be more efficient if the ethers are contained in one molecule rather than in several molecules of for example DME or diglyme.

Basically the same red shifts were achieved at high and low ether concentrations with tetraglyme and the higher molecular weight polyethers. Therefore, there is not much discernible difference between the complexing ability of these ethers toward tight ion pairs. This indicates that tetraglyme and the polymeric ethers are able to form equivalent complexes with approximately the same geometry and coordination number. Such a complex would be less energetically feasible with DME or diglyme due to unfavorable entropy requirements. These results moreover indicated that cation coordination is not strongly dependent on whether the ether oxygens are along the polymer backbone or in a pendant ligand.

A slight blue shift was found with the polyethers of molecular weight above 1000 compared to the largest

λ_{\max} values which were obtained with tetraglyme, PEO 600, and PEO 1000. This blue shift could be attributed to stacking of the picrate anions along the polymer chain as they remain in the vicinity of the complexed cations if the absorption decreased with ligand addition.⁶⁹ However, the absorption remained constant. This blue shift, therefore, could not be readily explained.

Viscometry

It is well known that the viscosity of polymer solutions is related to polymer dimension with an increase in chain dimensions resulting in an increase in viscosity. Lundberg, Bailey, and Callard interpreted the increase in viscosity of poly(ethylene oxide) in methanol on addition of alkali halide salts as due to chain expansion caused by binding of the anion to the polymer.³⁷ Since there is substantial evidence for binding of alkali cations to glymes, PEO, and crown ethers, it was decided to investigate the system further.^{2,3,8,10,25,35,59} Using a system of 2.5×10^{-2} M in monomer of PEO having a molecular weight of 6×10^6 g/mole with addition of 1.0×10^{-4} M to 1.0×10^{-1} M KBr in methanol, the results of Lundberg *et al.* could be reproduced, particularly the value of one salt molecule for every ten monomer units at maximum viscosity. This number, however, is calculated by assuming complete binding of all cations at maximum viscosity. The addition of tetramethylammonium bromide to PEO in methanol gave different results. Although the tetramethylammonium cation

should not bind to the polymer,⁵³ it was expected that increased viscosity would still be measured due to anion binding if Lundberg et al. were correct in their data interpretation. The negligible change in viscosity upon addition of tetramethylammonium bromide to PEO indicated that the cation is the ion bound to poly(ethylene oxide).

There are several processes which are expected to determine the dimensions of a poly(ethylene oxide) coil in the presence of alkali cation salts. These processes are shown in Figure 19. As alkali cations are bound to poly(ethylene oxide), positive charge density builds along the polymer chain. As this charge density increases, mutual charge-charge repulsions cause the polymer coil to expand. This expansion, if all other factors are negligible, would continue until the charge density is high enough to prevent more cations from entering the polymer domain. At the same time, however, anions are also being introduced into the vicinity of the polymer. At low salt concentration, they have little effect but as the salt concentration increases, the presence of these anions begins shielding the charge-charge repulsions of the cations along the chain. A third factor is the increased shielding at larger positive charge density due to the requirements of electroneutrality in the polymer domain.³⁶ As more cations are complexed by the polymer, the large charge density inside the polymer domain causes anions to move into the polymer domain reducing the high positive

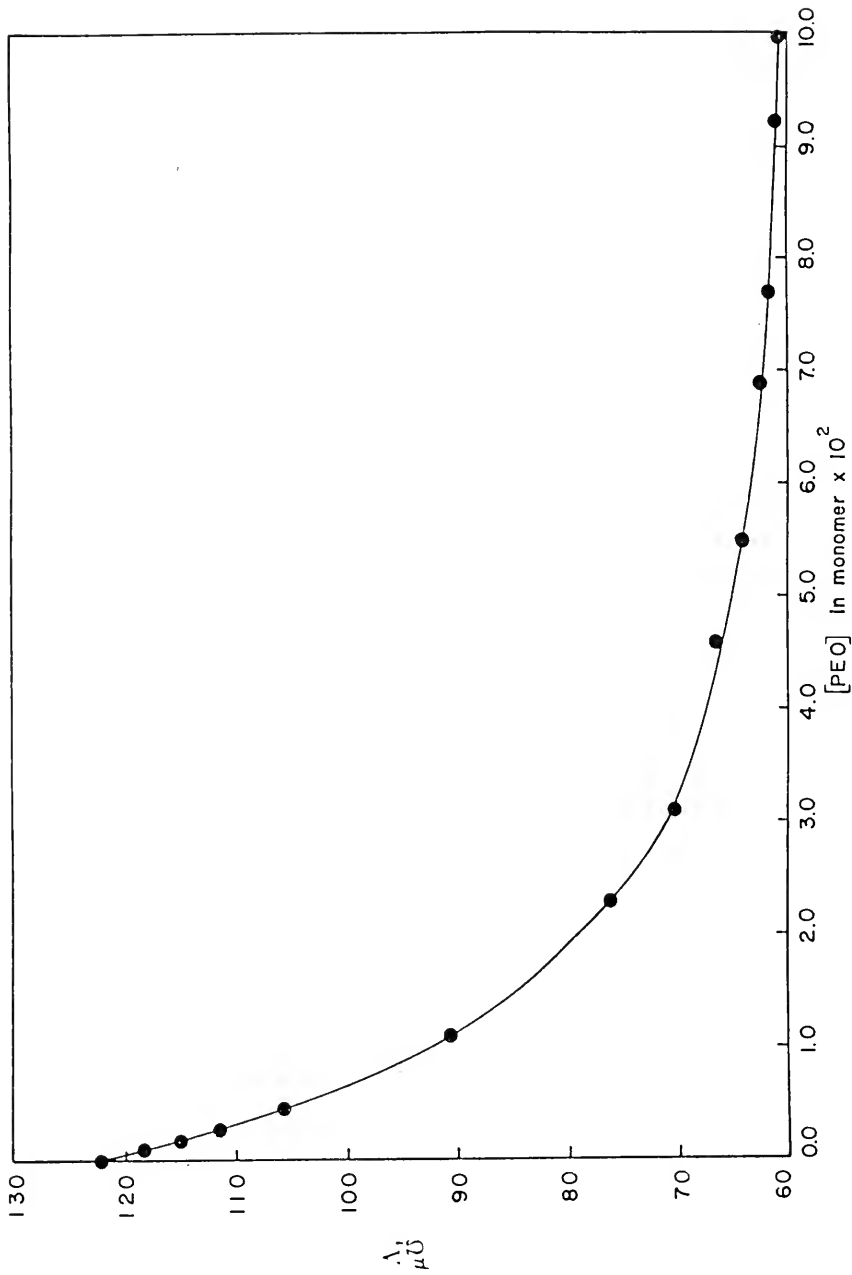


Figure 18. Conductance of 1.0×10^{-4} M NaBPh_4 + PEO 900,000 in CH_3CN at 25°

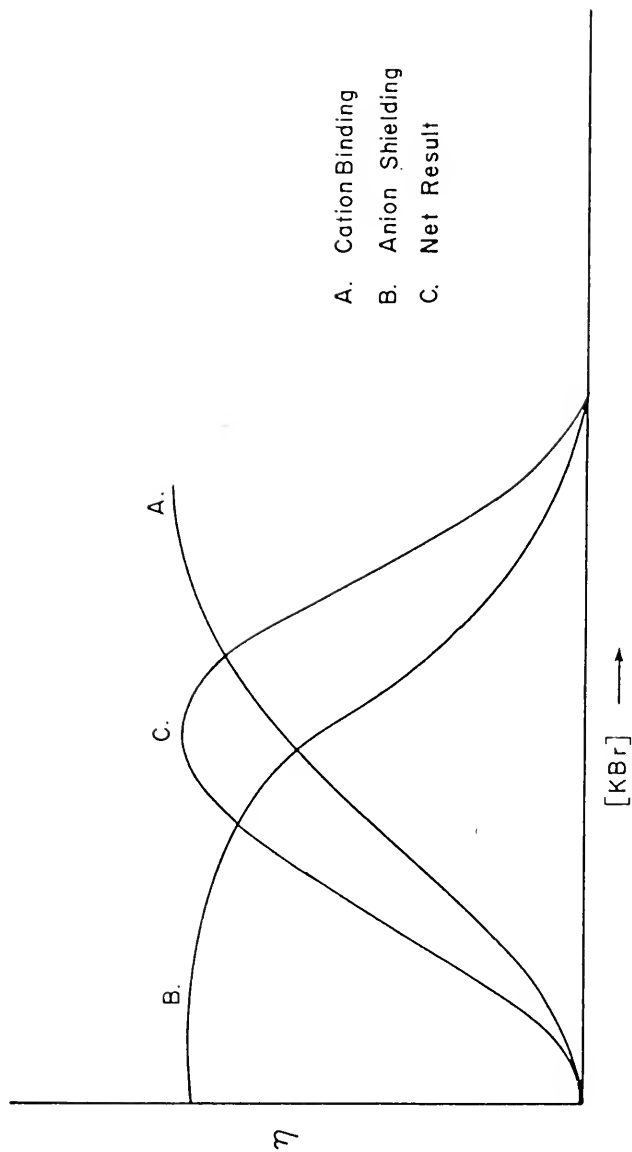


Figure 19. Effects of Alkali Metal Salts on PEO Viscosity

charge. The net result of these effects is an expansion of the polymer upon initial salt addition which reaches a maximum and then begins to decrease as shielding becomes very effective at high salt concentration.³⁶ This is demonstrated in Figure 4 with the addition of KBr to PEO of molecular weight 100,000 in methanol.

The effects of shielding become more evident upon comparison of the PEO/KBr system to the PEO/KBr system containing dicyclohexyl-18-crown-6. The 1:1 addition of crown ether to KBr in the PEO solution in methanol produced a viscosity reading equal to that of PEO in methanol without any added salt. This indicated that crown ether was able to effectively remove all potassium ions from the polymer domain due to its stronger binding ability. Therefore, the addition of crown ether to a solution of PEO and KBr in methanol allowed a viscosity study in which free K^+ was varied while the anion concentration remained constant (Figure 4). The crown ether system produced a curve in which the maximum was decreased and displaced to higher concentration of free potassium ions. The occurrence of a maximum indicates that shielding becomes more prominent as positive charge density increases along the chain at constant anion concentration. This is expected from the behavior of a typical polyelectrolyte system.³⁶ The decreased maximum indicates that the repulsions are reduced compared to the system without crown ether so that

the anion concentration appears to have a moderate effect on polycation shielding. The increase in salt concentration at maximum viscosity in the presence of crown ether may be due in part to more cations needed to produce a particular expansion at the high anion concentration, but this in itself should increase the number of anions attracted into the polymer domain. This particular effect is not well understood.

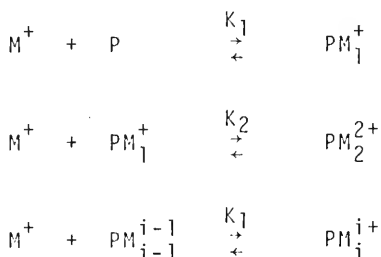
Potentiometry

A system similar to the one above was studied by ion-selective electrode potentiometry (Table 3). The basic differences here are a lower molecular weight PEO (100,000) and use of the chloride salt instead of bromide. The concentration of polymer and salt are in the same range here as with the viscosity studies but this system differs from the viscosity system because here polymer is added to the salt solution. The use of chloride anion was necessary because the Ag/AgCl reference electrode was susceptible to contamination by bromide ions. Upon addition of PEO from 1.14×10^{-2} M to 4.14×10^{-2} M in monomer to 1.0×10^{-3} M KCl in methanol, the number of monomer units per cation bound was found to increase from 29 to 43 as the amount of polymer increased. These values did not agree with that of ten monomer units per cation found in viscosity studies. Since both polymers are of high

molecular weight, it may be assumed that they would complex approximately the same number of cations for a particular number of monomer units. However, in viscosity studies of Lundberg *et al.* it was assumed that all added cations were bound to the polymer.³⁷ The potentiometry results indicated that this was not the case.

Conductance

The complexation processes involving the binding of cations to polymer chains may be described by the following equilibria:



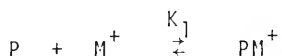
Here PM_1^+ represents the polymer containing only one cation and PM_i^{i+} represents the attachment of the i^{th} cation to this polymer chain. There may be large numbers of cations attached to a single chain in the high molecular weight polymers, but charge repulsions along the relatively small chains of the low molecular weight polymers reduce the chances of large numbers of cations binding to these systems.

The decrease of conductance of a salt solution upon addition of a polymer indicates coordination of one or more cations to the polymer resulting in a lowering of the ion mobilities (see Figure 11). This continues until all cations have been complexed. Addition of more polymer at this point should cause redistribution of cations from polymers containing more than one cation to polymers with no cations. This would be due to the higher energy of polymers containing more than one cation resulting from charge-charge repulsions along the polymer chain. At very high polymer concentration this redistribution due to $PM_i^{i+} + i P \rightleftharpoons i PM_1^+$ is virtually complete and the conductance is not expected to change upon further addition of polymer. The measured conductance is now the sum of the limiting conductance of a polymer chain carrying one cation $\lambda_{0,1}^+$ and the limiting conductance of the anion, λ_0^- .

Binding to PEO 1000. The simplest example of the conductance decrease is given with PEO 1000 which had a $1/R$ vs. $[polymer]$ conductance curve similar to that for 18-crown-6 in the complexation of $NaBPh_4$ in acetonitrile (Figures 8 and 11). In both cases, the initial section of the curve describing cation binding was nearly linear; however, the initial slope was much larger with the crown ether. The transition from this linear segment to a horizontal segment indicating one cation per ligand occurred

much higher in monomer concentration of PEO than with crown ether but was very rapid with both PEO 1000 and 18-crown-6. The lack of a prominent redistribution region with PEO 1000 indicated that the polymer probably complexed a very small number of cations per chain even at low polymer concentration, which was not unexpected due to the small size of the chain.

The binding constant K_1 for the complexation of one sodium cation to such a polymer may be calculated as follows:



The equivalent conductance for a system, λ , is defined as

$$\lambda = \frac{1000 \kappa}{cR}$$

where κ = the cell constant, c = the salt concentration and R = the solution resistance.⁷⁰

$$\frac{1}{R} = \frac{c}{1000 \kappa} \cdot \lambda = c \cdot f \cdot \lambda$$

Let R_0 be the resistance of the solution without added polymer; then,

$$\frac{1}{R_0} = c \cdot f \cdot \lambda_0 = c \cdot f (\lambda_0^+ + \lambda_0^-)$$

If α = the fraction of cations bound, then at a resistance R , the contribution to conductance of the cations complexed by the polymer = $c \cdot f \cdot \alpha \cdot \lambda_{0,1}^+$, and the contribution of free ions = $c \cdot f \cdot (1 - \alpha) \lambda_0^+$.

Therefore,

$$\frac{1}{R} = c \cdot f [(1 - \alpha) \lambda_0^+ + \alpha \lambda_{0,1}^+ + \lambda_0^-]$$

$$\frac{1}{R_0} - \frac{1}{R} = f \cdot c \cdot \alpha (\lambda_0^+ - \lambda_{0,1}^+) = \alpha \Delta$$

$$\alpha = \frac{[PM^+]}{[PM^+] + [M^+]}$$

$$K_1 = \frac{[PM^+]}{[P][M^+]} = \frac{\alpha \cdot c}{[P][1 - \alpha]c}$$

Therefore,

$$\alpha = \frac{K[P]}{K[P] + 1}$$

so that

$$\frac{1}{R_0} - \frac{1}{R} = \Delta (1/R) = \frac{K[P]}{K[P] + 1} \cdot \Delta$$

where

$$\Delta = \frac{1}{R_{\text{salt}}} - \frac{1}{R_{\text{limit}}}$$

$$\left(\frac{1}{R}\right) = \frac{1}{R_{\text{salt}}} - \frac{1}{R_{\text{salt}} + \text{polymer}}$$

so,

$$\frac{\Delta}{\Delta(1/R)} = \frac{1}{K} \cdot \frac{1}{[P]} + 1$$

Thus a plot of $\Delta/\Delta(1/R)$ vs. $1/[P]$ is expected to give a line with slope = $1/K$. The plot for PEO 1000 over a free polymer concentration range of 8.81×10^{-5} - 4.84×10^{-5} M is given in Figure 20. The line was found to have a slope of 1.33×10^{-4} and a value of $K_1 = 7.52 \times 10^{-3}$.

Binding to PEO 6000. Poly(ethylene oxide) of molecular weight 6000 had a $1/R$ vs. [polymer] conductance plot similar in many respects to that of PEO 1000 (Figure 11). The initial slopes of both curves are very close with PEO 1000 having a slightly larger slope. Also, the concentration in monomer units at which PEO 1000 levels off at limiting conductance is just below the concentration where PEO 6000 begins to approach its limiting

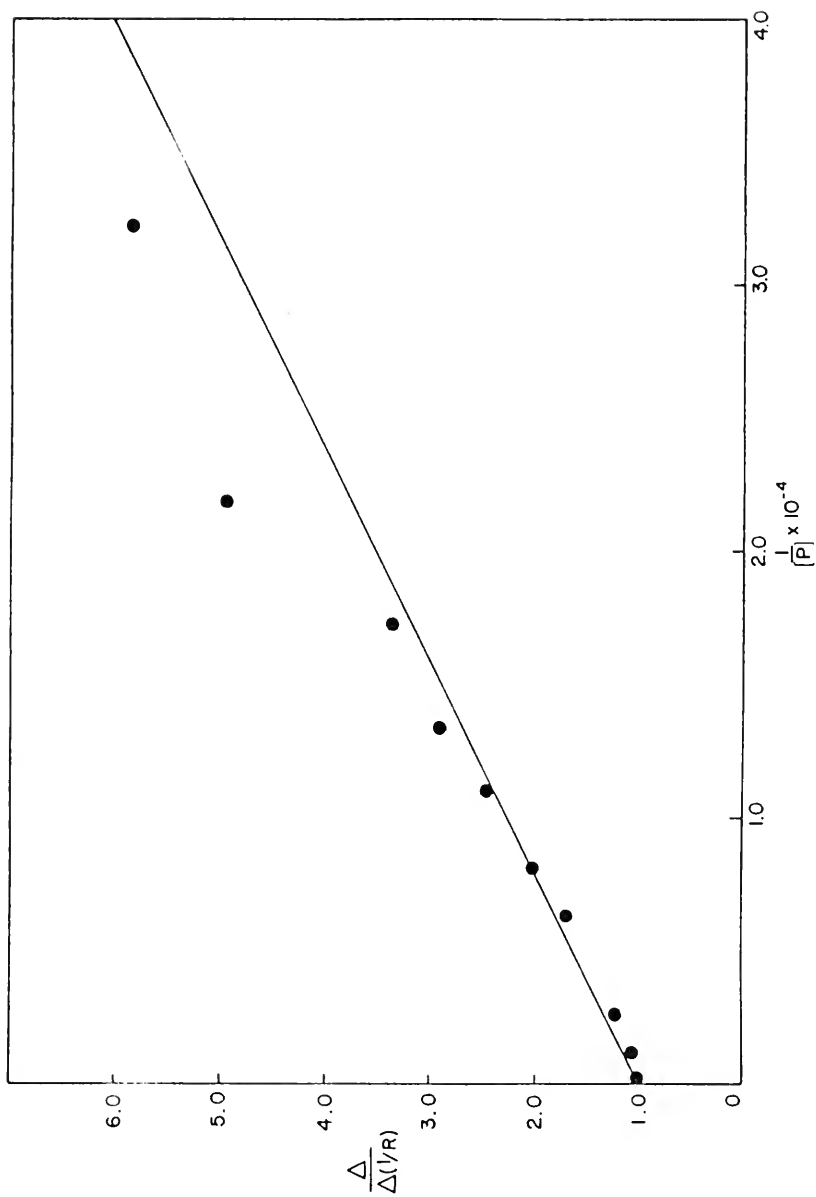


Figure 20. $\Delta/\Delta(1/R)$ vs. $1/[P]$ for PEO 1000 K₁ Calculation

conductance (Table 9). Unlike PEO 1000, as more PEO 6000 is added in the region following complete complexation, there is a gradual decrease in conductance. This indicates that all the cations are indeed bound to polymer chains but some cations are being redistributed (see below).

The complexation constant for the binding of one cation to a polymer may be calculated as with PEO 1000. The $\Delta/\Delta(1/R)$ vs. $1/[P]$ plot is shown in Figure 21. The curvature at low polymer concentration is due to more than one cation being complexed per polymer chain. The results of this plot are shown in Table 11 where they are compared to the values for PEO 1000.

Table 11. K_1 for NaBPh_4 + PEO 1000 and 6000 in Acetonitrile

Polymer	Slope	K_1
PEO 1000	1.33×10^{-4}	7.52×10^3
PEO 6000	1.35×10^{-5}	7.41×10^4

The increased binding constant for the larger molecular weight polymer is expected for statistical reasons. This may be explained from the following.

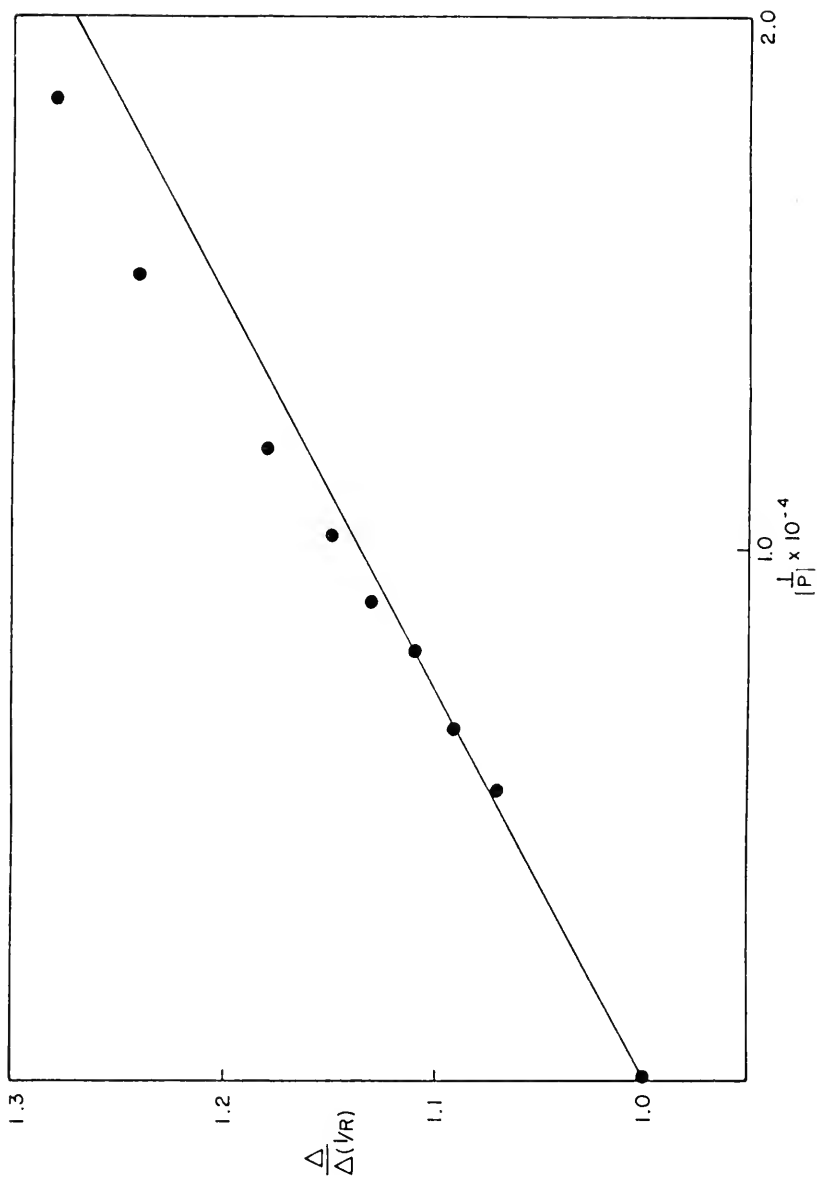


Figure 21. $\Delta/\Delta(1/R)$ vs. $1/[P]$ for PE0 6000 K_1 Calculation

Let $K_{1000} = K_1$ for PEO 1000 and $K_{6000} = K_1$ for PEO 6000.

$$\frac{K_{1000}}{K_{6000}} = \frac{e^{-\Delta G_{1000}/RT}}{e^{-\Delta G_{6000}/RT}}$$

$$\begin{aligned} \ln \frac{K_{1000}}{K_{6000}} &= -\frac{\Delta G_{1000}}{RT} - \left(-\frac{\Delta G_{6000}}{RT}\right) = \\ &= \frac{-\Delta H_{1000} - \Delta H_{6000}}{RT} + \frac{\Delta S_{1000} - \Delta S_{6000}}{R} \end{aligned}$$

Since the cation in each polymer is being complexed to a site which is equivalent physically to that in the other polymer,

$$\Delta H_{1000} \approx \Delta H_{6000}$$

$S \sim k \ln W$, where W is the possible number of ways to complex the cation.

Since

$$\begin{aligned} \frac{\Delta S_{1000} - \Delta S_{6000}}{R} &= \ln W_{1000} - \ln W_{6000} \\ &= \ln \frac{W_{1000}}{W_{6000}} \end{aligned}$$

therefore,

$$\frac{K_{1000}}{K_{6000}} = \frac{W_{1000}}{W_{6000}}$$

The total number of possible ways to coordinate the cation with the polymer is given by $W = q![p!(q - p)!]$, where q represents the number of oxygen atoms per polymer molecule and p the average number of oxygen atoms coordinated to the cation. However, not all combinations of oxygen atoms are equally probable. When ethers in the chain of a polymer are separated by more than two carbon atoms, the solvating power of the polymer decreases sharply. Therefore, only those combinations involving consecutive coordination sites are important. The number of these is $W = q - p + 1$.⁷¹

For sodium, the coordination number $p = 5$. PEO 1000 has 22 oxygen atoms with $W_{1000} = 18$. PEO 6000 has 136 oxygen atoms giving $W_{6000} = 132$. Therefore, the calculated $K_{6000} = 7.3 K_{1000}$. From experimentally determined binding constants, it was found that $K_{6000} = 9.85 K_{1000}$.

The small decrease in conductance noted at high polymer concentration on the $1/R$ vs. [polymer] conductance plot for PEO 6000 has been described as resulting from cation distribution from a polymer containing more than one cation to a polymer containing no cations.

This process may be described as follows:



$$K^* = \frac{[\text{PM}_2^{2+}][\text{P}]}{[\text{PM}_1^+]^2} = \frac{K_2}{K_1}$$

Assuming the absence of unbound cations, we can write

$$\text{the salt concentration} = \text{PM}_1^+ + 2 \text{ PM}_2^{2+}.$$

The fraction of salt complexed as the dication,

$$\beta = \frac{2[\text{PM}_2^{2+}]}{[\text{PM}_1^+] + 2[\text{PM}_2^{2+}]}$$

so that

$$[\text{PM}_2^{2+}] = \frac{\beta}{2} \cdot c$$

Now,

$$\frac{1}{R} = f \cdot c [(1 - \beta) \lambda_{0,1}^+ + \beta \lambda_{0,2}^{2+}]$$

where $\lambda_{0,2}^{2+}$ is the limiting conductance of a polymer chain carrying two cations. $\lambda_{0,2}^{2+}$ is dependent on the mobility

of polymeric PM_2^{2+} . If it is assumed that there is no change in polymer size upon adding a second cation, the limiting conductance of a polymer containing two cations, $\lambda_{0,2}^{2+}$, should be $\sim 2\lambda_{0,1}^+$.

Thus,

$$\frac{1}{R} = f \cdot c(1 + \beta)\lambda_{0,1}^+$$

Since

$$K^* = \frac{[(\beta/2) \cdot c][P]}{[1 - \beta]^2 c^2}$$

$$2K^*c^2(1 - \beta)^2 = \beta cP$$

Now if $\beta \ll 1$,

$$\beta = \frac{2K^*c}{[P]}$$

Substituting for β and differentiating $1/R$ with respect to $1/P$, we obtain

$$\frac{\Delta(1/R)}{\delta(1/[P])} = f \cdot c \lambda_{0,1}^+ \left(\frac{\delta\beta}{\delta(1/[P])} \right) = 2fc^2\lambda_{0,1}^+ K^*$$

A plot of $1/R$ vs. $1/[P]$ over the polymer concentration range of 3.3×10^{-2} M to 1.0×10^{-1} M in monomer

PEO 6000 where no free ions are present gave a straight line with a slope = $2fc^2K^*\lambda_{0,1}^+$ (Figure 22). K^* was then calculated and since $K^* = K_2/K_1$, K_2 was also calculated. It should be noted that the plot was not linear for polymer concentrations below the range listed above. This deviation is probably due to complexation of more than two cations per polymer causing $1/R$ to be lower than expected. The results for PEO 6000 are given in Table 12.

Table 12. Binding Constants for Complexation of Na^+ to PEO 6000 in CH_3CN

Polymer	K_1	Slope of $1/R$ vs. $1/[P]$	K^*	K_2
PEO 6000	7.41×10^4	8.18×10^{-4}	0.235	1.74×10^{-4}

Binding to high molecular weight polymers. The higher molecular weight polymers, PEO 100,000 and PEO 900,000, gave different $1/R$ vs. $[PEO]$ conductance plots upon addition to salt solutions than the lower molecular weight polymers (Figures 11 and 12). PEO 100,000 had an initial slope slightly larger than PEO 900,000 but quite surprisingly both of these slopes were significantly smaller than the slopes of PEO 1000 and 6000. Also, in

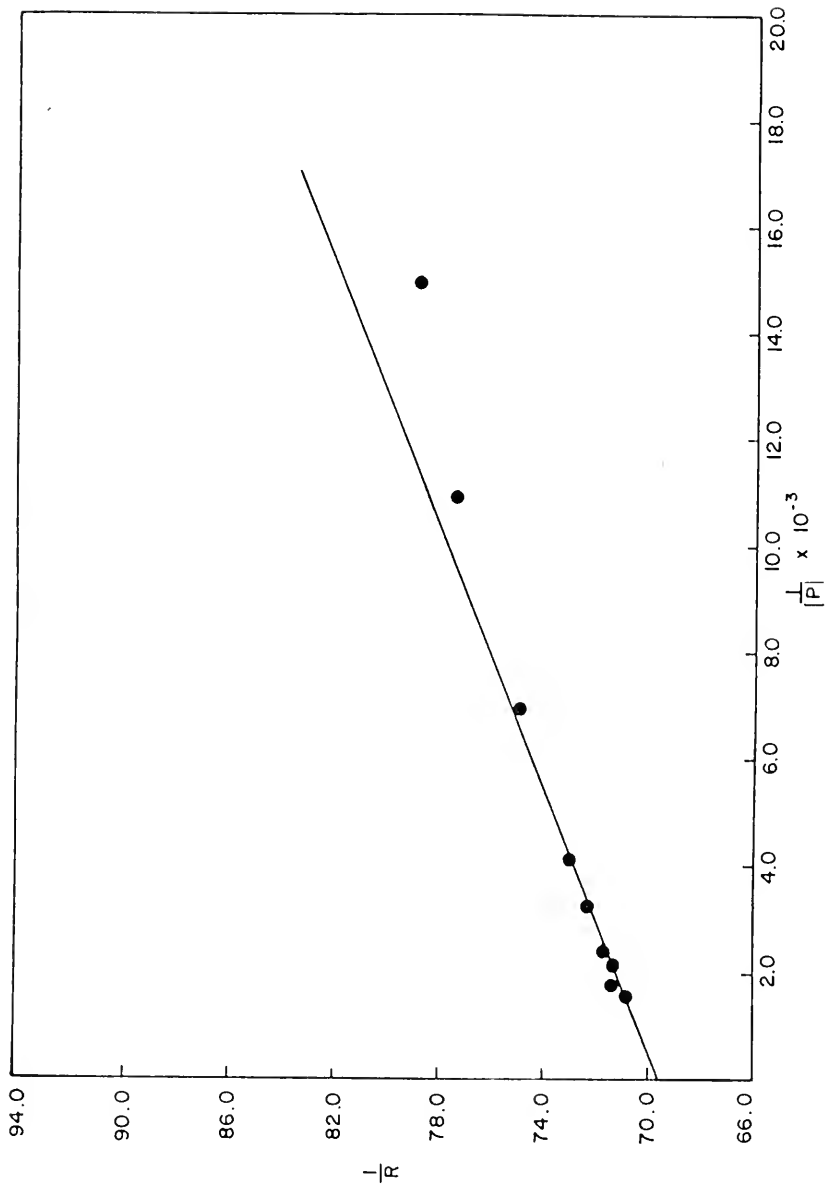


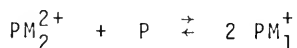
Figure 22. $\frac{1}{R}$ vs. $\frac{1}{[P]}$ for PEO 6000 K_2 Calculation

contrast to PEO 1000, the high molecular weight polymers did not approach a horizontal line at high polymer concentration, but instead both showed a continual decrease. These decreases at high polymer concentration with the high molecular weight polymers were much larger than with PEO 6000. Furthermore, the conductance of the PEO 100,000 and 900,000 solutions at high polymers concentration was much lower than the conductance of the PEO 1000 and 6000 systems.

At low polymer concentration, the slopes decreased with increasing molecular weight. This can be explained by considering two factors. First, viscosity measurements indicate that at these salt concentrations ($\sim 10^{-4}$ M), the size of the polymers is not greatly changed on cation binding so that the conductance per ion increases with the molecular weight assuming a constant number of ethylene oxide units per cation site. Second, the mobility of polymers in solution decreases with molecular weight but this decrease is less than linear. For instance, for a random walk polymer the diffusion coefficient varies as $M^{-1/2}$.⁷¹ Therefore the equivalent conductance of polymer bound cations is expected to increase with molecular weight. This leads to lower slopes at low polymer concentration for higher molecular weight polymers.

At high polymer concentration, the magnitudes of the slopes were found to increase with increasing molecular

weight. After all cations had been complexed, the lower molecular weight polymers, due to their small size, contained relatively few cations per polymer. As more polymer was added there were relatively few cations transferred to the uncomplexed polymer chains due to the low concentration of PM_2^{2+} in the following equilibrium:



The low number of cations transferred caused little change in transport of charges or mobility of polymer bound cations. With the high molecular weight polymers, assuming constant binding of cations per unit weight for all polymers, there were many cations per polymer chain. As more high molecular weight polymer is added, there were many cations redistributed from polymers containing many cations to polymers containing fewer numbers of cations. This led to a greater decrease in conductance than with the lower molecular weight polymers.

There were several factors which caused difficulty with the calculation of binding constants with the higher molecular weight polymers. Since the polymers are so large and so many cations can be bound per polymer chain at low polymer concentration, the binding and redistribution processes occur simultaneously over most of the polymer concentration range. This leads to many equilibria

being established which cannot be properly evaluated. The binding processes themselves, as can be shown from earlier calculations, would lead to an expression for conductance which can be described as follows:

$$\frac{1}{R} = f \cdot c [(1 - \beta) \lambda_0^+ + \beta_1 \lambda_{0,1}^+ + \frac{\beta_2}{2} \lambda_{0,2}^+ + \dots + \frac{\beta_i}{i} \lambda_{0,i}^+ + \dots]$$

where β_i is the fraction of salt complexed to the polymers containing i cations. It is clearly impractical to evaluate the binding constant K_i using this equation.

In addition, complications arise from probable site binding of counterions to the polycation.⁷² Such effects were evident from the work of Lundberg, Bailey, and Callard, who showed specific anion effects on the viscosity of cation bound poly(ethylene oxide).³⁷ Similar anion effects have been observed in light scattering experiments on these systems.⁵⁸ Thus a quantitative or even semiquantitative description of these high molecular weight polymers is difficult on the basis of the above conductance methods.

Mobility of PM_1^+ complexes. For the low molecular weight PEO 1000, it is possible to calculate $\lambda_{0,1}^+$, the limiting conductance of the polymer containing one cation. As was apparent from a comparison between the 18-crown-6 and PEO 1000 $1/R$ vs. $[PEO]$ conductance curves

at high polymer concentration, it is reasonable to assume only one sodium ion per polymer. It has been shown that

$$\frac{1}{R_0} = c \cdot f \cdot \lambda_0 = c \cdot f (\lambda_0^+ + \lambda_0^-)$$

where $\lambda_{0,Na^+}^+ = 77.3$ and $\lambda_{0,BPh_4^-}^- = 58.1$ in acetonitrile.⁶⁷ At the limiting conductance,

$$\lambda_0 = \lambda_{0,1}^+ + \lambda_0^-$$

Therefore,

$$\frac{1}{R_0} - \frac{1}{R} = c \cdot f (\lambda_0^+ - \lambda_{0,1}^+)$$

so that

$$\lambda_{0,1}^+ = \frac{(1/R_0) - (1/R)}{c \cdot f} - \lambda_0^+$$

For PEO 1000, $\lambda_{0,1}^+ = 36.6$.

For PEO 6000, it was shown for the K_2 calculation that a plot of $1/R$ vs. $1/[P]$ gave a straight line (Figure 22). The intercept of this plot at $[PEO] \rightarrow 0$ gives the limiting conductance $\lambda_{0,1}^+ + \lambda_0^-$ which equals 69.6. Subtracting the value of λ_0^- for BPh_4^- gives a value of 11.5 for $\lambda_{0,1}^+$ for PEO 6000.

Since the $\lambda_{0,1}^+$ values are a function of the mobility of polymer bound cations, if a randomly coiled polymer is assumed they should be related by $M^{-1/2}$ where M is the molecular weight.⁷¹ The ratio of $\lambda_{0,1}^+$ for PEO 1000 and 6000 is 3.18 compared to the ratio of their molecular weights of 2.45. Although this method does not give the exact relationship between $\lambda_{0,1}^+$ values for various molecular weight polymers, it can nevertheless be used to approximate $\lambda_{0,1}^+$ for the high molecular weight polymers. For PEO 100,000 the $\lambda_{0,1}^+$ value is found to be approximately 3.2 and for PEO 900,000 it is approximately 1.2. Therefore, at high polymer concentration of high molecular weight polymers $1/R$ approaches λ_0^- .

Discussion of Poly(3,6,9,12,15-pentaoxa-1-heptadecene)

From inspection of Table 6, it appears that the λ_{\max} of sodium picrate in 10% THF/ CHCl_3 in the presence of P(PHD) was the same as that for equal quantities in terms of monomer units of poly(ethylene oxide). As stated earlier for poly(ethylene oxide), the relative shifts involved led to the conclusions that the polymers are only peripherally solvating the sodium cation in this solvent and that ion pair complexation constants are about the same as with PEO.

From the conductance data of P(PHD), Figure 16, the P(PHD) concentration at which the conductance curve approaches a "constant level" was approximately 3.0×10^{-2} M in monomer in acetonitrile which was very close to the value of 2.6×10^{-2} M in monomer for PEO 1000. This is further evidence for the similarity of the binding constants of P(PHD) and PEO. The $1/R$ conductance value where the curve approaches a "horizontal" line, however, was much higher with P(PHD) than with any of the PEO polymers. For example, the P(PHD) plot began to level off at a value of $90.79 \mu\Omega$, whereas PEO 100,000 was still decreasing slightly at $60.6 \mu\Omega$. Since the sodium cation may be effectively complexed in a 1:1 stoichiometry by a glyme containing five oxygens, it may be coordinated to a single pendant ligand on P(PHD).² In order for a complexed sodium ion to move along this polymer chain, it would only be necessary to shift from one pendant glyme to an adjacent one without involving a major conformational change in the polymer. With PEO, however, a conformational change in the polymer chain would be required to move a sodium ion from a binding site composed of five oxygen atoms in the polymer backbone to another site farther along the polymer containing another five oxygen atoms in the proper conformation. From entropy considerations, transport of a sodium ion along the chain would be easier with P(PHD) which would lead to a higher limiting conductance.

Solvent Effects

From conductance studies in various solvents, P(PHD) demonstrated stronger complexation of sodium ions in THF, followed by acetonitrile and then acetone (Table 10). This trend is not due primarily to any typical polymer effects since the results with acetone and acetonitrile correspond to the results obtained by adding 18-crown-6 to NaBPh_4 in the same solvents (Figures 8 and 9 and Table 9). In the polymer study, the THF sample exhibited the largest slope but had a much smaller $\Delta[(1/R_0) - (1/R)]$. This indicates that THF coordinates the sodium cation very strongly; however, since NaBPh_4 exists primarily as ion pairs at 1.0×10^{-4} M in THF, complexation of the salt to a polymer would increase the ion separation leading to higher conductance.^{43,64} Therefore, complexation of the salt would not be expected to give a large drop in conductance. The above trend for acetonitrile and acetone is hard to justify in terms of commonly used parameters such as the Gutmann donor number or dipole moment since acetone has a higher donor number than acetonitrile but acetonitrile has a higher dipole moment. The overall solvent effect is probably the result of a combination of solvent basicity and dipole moment.

Cation Effects

In conductance studies in both acetonitrile and THF, larger slopes were found for complexation of sodium ions by P(PHD) than for potassium ions (Table 9). This indicates sodium selectivity, which agrees with the fact that the monomeric analog of P(PHD), tetraglyme, was found to have a higher equilibrium constant with sodium ions than with potassium ions in the formation of separated ion pairs of fluorenyl salts in THF. The value for sodium was 170 vs. 0.35 for potassium.²

Discussion of Poly(acryloyltyrocidine)

For reasons outlined in the Results section, quantitative analysis of poly(acryloyltyrocidine) was very difficult. The insolubility of this polymer in aqueous media made possible the use of extraction equilibria to determine the cation binding ability and selectivity. This was the only polymer which could be studied in this manner. Poly(acryloyltyrocidine) was found to transfer larger amounts of sodium picrate than potassium picrate from an aqueous layer into a chloroform layer containing the polymer and thus appeared to be sodium selective. The cesium cation was found to be too large to be complexed by the cyclic antibiotic.

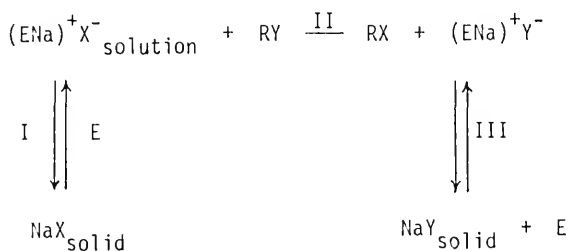
CHAPTER III

PHASE TRANSFER REACTIONS

As mentioned previously, polymers which act as catalysts in organic reactions have many advantages over low molecular weight catalysts. For example, with reactions involving alkali metal salts, polymers may act as catalyzing agents by complexing cations to an extent which in many cases is as strong or stronger than the corresponding low molecular weight analogs or by interacting with solid phase reagents in a manner more energetically favorable than low molecular weight compounds. From the information obtained on binding of cations to nonionic polymers, it may be possible to obtain additional insight into the polymeric catalysis of reactions involving alkali metal salts.

Many alkali or alkali earth salts have been used in organic syntheses, but because of their limited solubility in organic solvents, their use was frequently under inefficient conditions such as low concentrations or two-phase operations.⁵⁹ Following Pedersen's discovery that crown ethers formed complexes with alkali metal salts that were soluble in aprotic solvents due to

this complexation, attention has been focused toward utilizing the anion of the complex for synthetic purposes.²⁹ It was previously found in these solvents that crown ethers could complex the cation strongly enough to reduce the degree of interaction between the cation and anion of contact ion pairs.^{73,74} In organic aprotic solvents where they were unencumbered by strong solvation processes, many of these anions have proven to be strong nucleophiles.^{27,31} The general reaction scheme is shown in the following set of equations for a heterogeneous system:



where RY is a typical alkali halide substrate, $(\text{ENa})^+\text{Y}^-$ is a crown ether complexed alkali metal salt, and RX is the product of the nucleophilic attack of X^- on RY.

Since strong cation coordination played such an essential role in phase-transfer reactions, it was anticipated that the various polyethers would catalyze phase-transfer reactions to the same relative extent to which they coordinated alkali cations. The reaction chosen for

studying this process was the nucleophilic displacement of bromide anion from an alkyl bromide by acetate anion in acetonitrile. This reaction involved sodium acetate which was insoluble in acetonitrile, butyl bromide, and the following polyethers all of which were soluble in this solvent: DME, diglyme, tetraglyme, poly(ethylene oxide) of various molecular weights, poly(3,6,9,12,15-pentaoxa-1-heptadecene), 18-crown-6, and poly(vinylbenzo-15-crown-5). Poly(vinylpyrrolidone) was also studied in order to compare the coordinating ability of another type complexing site. The acetate salt was chosen because of the most commonly used nucleophilic anions in acetonitrile, acetate is the most effective.²⁸ Also, in phase-transfer reactions involving the acetate anion in acetonitrile, virtually no alkene elimination product could be detected. Butyl bromide was chosen as the substrate since bromides proved to be more reactive than the corresponding tosylates or chlorides in this system.³¹ In addition, butyl acetate had a sufficiently low boiling point to facilitate analysis by gas chromatography. The ability of polymers to catalyze this reaction was further studied in homogeneous media by adding 5% water to each system. This allowed comparison of polymer catalysis in which the polymer had to interact with an insoluble salt matrix with catalysis in which the salt was already in solution. The percent yields were measured with gas chromatography

by comparing the peak areas of butyl acetate and butyl bromide.

Homogeneous Reactions

Results

The simplest case of polymer-catalyzed reactions would involve only step II of the scheme presented above. This would be a homogeneous reaction involving complexation of salt molecules already in solution. It was found that upon addition of 5% water to the mixture of 0.037 M butyl bromide, 0.096 M sodium acetate and polyether catalyst in acetonitrile, sodium acetate dissolved completely giving homogeneous solutions. Here, the catalyst did not have to interact with the surface of a salt matrix, but possible complications due to water catalysis had been introduced. In order to examine this problem, the reaction of sodium acetate and butyl bromide was carried out in acetonitrile containing various amounts of water. No additional catalyst was added. The results are given in Table 13.

Water is shown to catalyze the reaction to a significant extent. Apparently the effect levels off above 10% water. Also, the reaction does not proceed farther after two days. These results indicate that an equilibrium may be present which prevents the reaction from going to completion.

Table 13. 3.7×10^{-2} M Butyl Bromide + 9.6×10^{-2} M Sodium Acetate in Acetonitrile with H_2O Added

Percent H_2O	Percent Reaction ($\pm 3\%$)				
	5 hrs	8 hrs	1 day	2 days	3 days
5	15	16	32	54	58
10		47	76	84	83
20		48	80	85	85

The dependence on polyether concentrations was examined with P(PHD) and also tetraglyme in the homogeneous reaction media. In both cases, there were virtually no changes in product yield over the concentration range of 1.6×10^{-1} to 2.5 M in monomer P(PHD) and from 1.8×10^{-1} to 2.7 M tetraglyme with 3.7×10^{-4} M butyl bromide and 9.6×10^{-2} M sodium acetate.

The reaction of butyl bromide and sodium acetate catalyzed by the various polyethers was carried out in acetonitrile containing 5% water. Here the catalytic ability of the polyethers was expected to depend primarily on their ability to effectively coordinate the sodium cation. The results of these reactions are given in Table 14 and Figure 23.

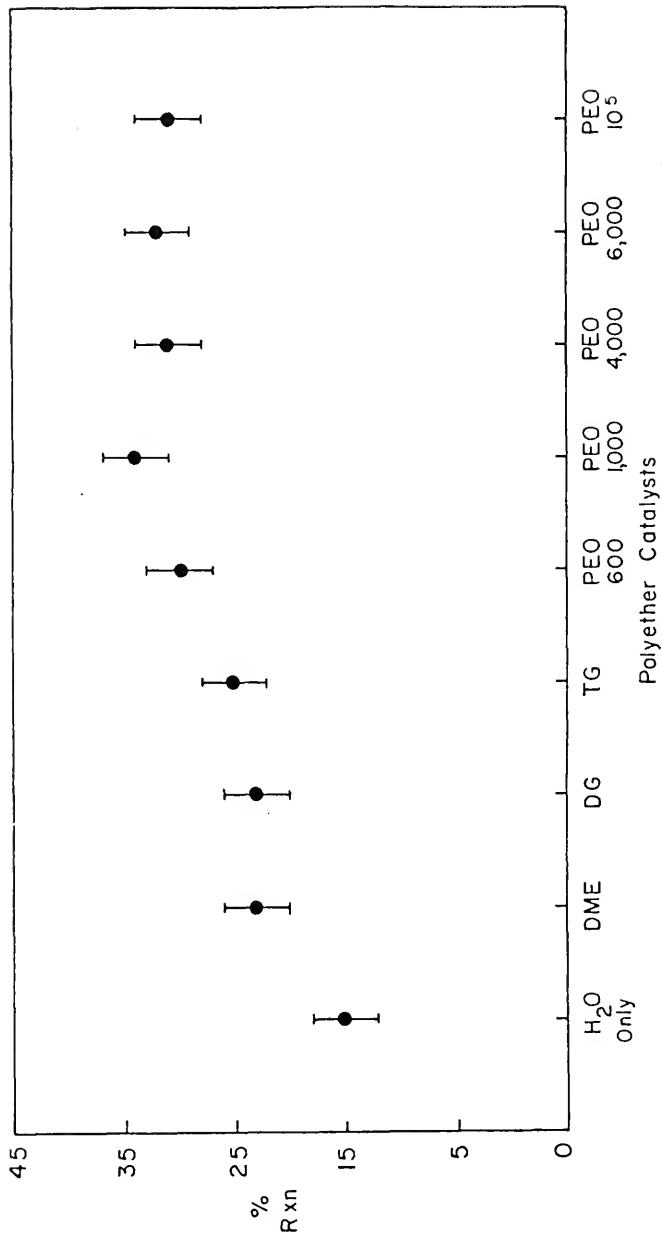


Figure 23. Butyl Bromide + Sodium Acetate in 5% H₂O/95% CH₃CN After 5 Hours

Table 14. 3.7×10^{-2} M Butyl Bromide + 9.6×10^{-2} M Sodium Acetate Catalyzed by 0.18 M Polyethers in Monomer in 5% $H_2O/95\%$ CH_3CN

Polyether	Percent Reaction ($\pm 3\%$)		
	5 hrs	1 day	3 days
DME	23	69	76
Diglyme	23	67	75
Tetraglyme	25	67	80
PEO 600	30	73	82
PEO 1000	34	86	80
PEO 4000	31	76	84
PEO 6000	32	--	83
PEO 10^5	31	78	81
PEO 3×10^5		77	86
PEO 9×10^5		77	87
P(PHD) 40,000 (1.0 M)			70

Since the results for one and three days are relatively close together, the reactions must be approaching equilibrium after one day. Therefore, the results after five hours should give a better indication of relative catalytic abilities. The maximum catalytic ability was achieved with PEO 1000 with the other polymers all giving slightly lower amounts of product.

Discussion

It is apparent from the results that an equilibrium exists in the homogeneous system which prevents the reactions from going to completion. This equilibrium condition is being approached after one day due to the similarity of results for one and three days. The fact that an equilibrium does exist in the presence of water indicates that water may have a "leveling effect" on the nucleophilicities of the acetate and bromide ions.⁷⁵ Hydrogen bonding by water may cause the nucleophilicities of the anions to become similar, allowing the reverse reaction to take place.

The data indicate that the low molecular weight glymes, DME and diglyme, catalyze the reaction to a lesser extent than the polymeric ethers. This correlates well with the UV-visible and conductance studies on cation binding. As shown earlier, DME and diglyme have a weaker complexing ability toward sodium cations than PEO due to a more negative entropy of binding.

There is very little difference among the various high molecular weight polyethers in their catalytic ability in the presence of water. This may be the result of efficient coordination of the cation by water molecules. This strong solvation by water may interfere with the binding process in a manner that would equalize the binding ability of the various molecular weight polymers resulting in approximately the same yields for each molecular weight.

Heterogeneous Reactions

Results

A heterogeneous reaction involves removal of salt from a solid matrix by the catalyst, sufficient coordination of the salt by the catalyst to activate the anion, and then depositing of the byproduct salt out of the solution phase. The same reaction examined in the homogeneous reaction section but without water present was found to proceed through these steps.

It has been found by using flame photometry that the solubility of potassium acetate in pure acetonitrile at 25°C is 5.0×10^{-4} M.³¹ Although in the present study sodium acetate is used and the acetonitrile solution is maintained at reflux temperature, visual observation indicates that the concentration of sodium acetate which

dissolved without complexation was not significant when compared to the overall salt concentration of 9.6×10^{-2} M used in these reactions.

In the reaction of 3.7×10^{-2} M butyl bromide with 9.6×10^{-2} M sodium acetate catalyzed by 1.0 M P(PHD) or 1.8×10^{-1} PEO 600, both polymers gave linear plots of $\log [\text{butyl bromide}]$ vs. time, indicating the reactions were first order in butyl bromide. The reaction order in salt could not be determined because of the low solubility of sodium acetate in acetonitrile. No significant concentration dependence was found for the polyethers P(PHD) and tetraglyme over the range 1.6×10^{-1} M to 2.0 M in monomer.

The relative efficiency of the various polyethers in catalyzing the reaction between butyl bromide and sodium acetate was measured in acetonitrile. The results are presented in Table 15.

At this polyether concentration the higher molecular weight polymer solutions were too viscous for gas chromatographic analysis. For the glymes and poly(ethylene oxide) polymers, maxima are apparent for the 600 and 1000 molecular weight polymers. Poly(pentaoxa-1-heptadecene), in which the oxygens are on ligands pendant to the polymer backbone, gave catalytic results comparable to the higher percentage PEO polymers.

In order to compare the efficiencies of the higher molecular weight poly(ethylene oxides), the glymes and

Table 15. Polyether Catalyzed Reactions of 3.7×10^{-2} M Butyl Bromide + 9.6×10^{-2} M Sodium Acetate in Acetonitrile

Polyether (1.0 M in monomer)	Percent Reaction (\pm 3%)	
	3 days	4 days
No catalyst	11	
DME ^a	43	58
Diglyme	28	46
Tetraglyme	39	65
PEO 600	64	78
PEO 1000	59	78
PEO 4000	52	
PEO 6000	49	
P(PHD)	55	

^aThe values for DME are proportionally higher than values measured later at lower concentration. Experimental error may be involved here.

PEO samples were run at lower polymer concentration, 1.8×10^{-1} M in monomer units. The results are given in Figure 24. Here again the highest conversion was achieved with PEO 1000 followed by a gradual decrease in product as the molecular weight increased.

The catalytic abilities of various other polymers were examined in this heterogeneous media. The results are given in Table 16.

Table 16. Reaction of 3.7×10^{-2} M Butyl Bromide with 9.6×10^{-2} M Sodium Acetate in CH_3CN Catalyzed by Various Polymers

Polymer (1.0 M in monomer)	Reaction Time	Percent Yield (\pm 3%)
P(PHD)	4 days	49
P(PHD) under dry N_2	4 days	52
Poly(vinylpyrrolidone)	4 days	77
PEO 600	4 days	78
PEO 1000	4 days	78

Catalysis by P(PHD) was not significantly changed when traces of water were removed from the system. Poly(vinylpyrrolidone) apparently had a catalytic ability similar to PEO 600 and 1000 which were the most effective PEO catalysts.

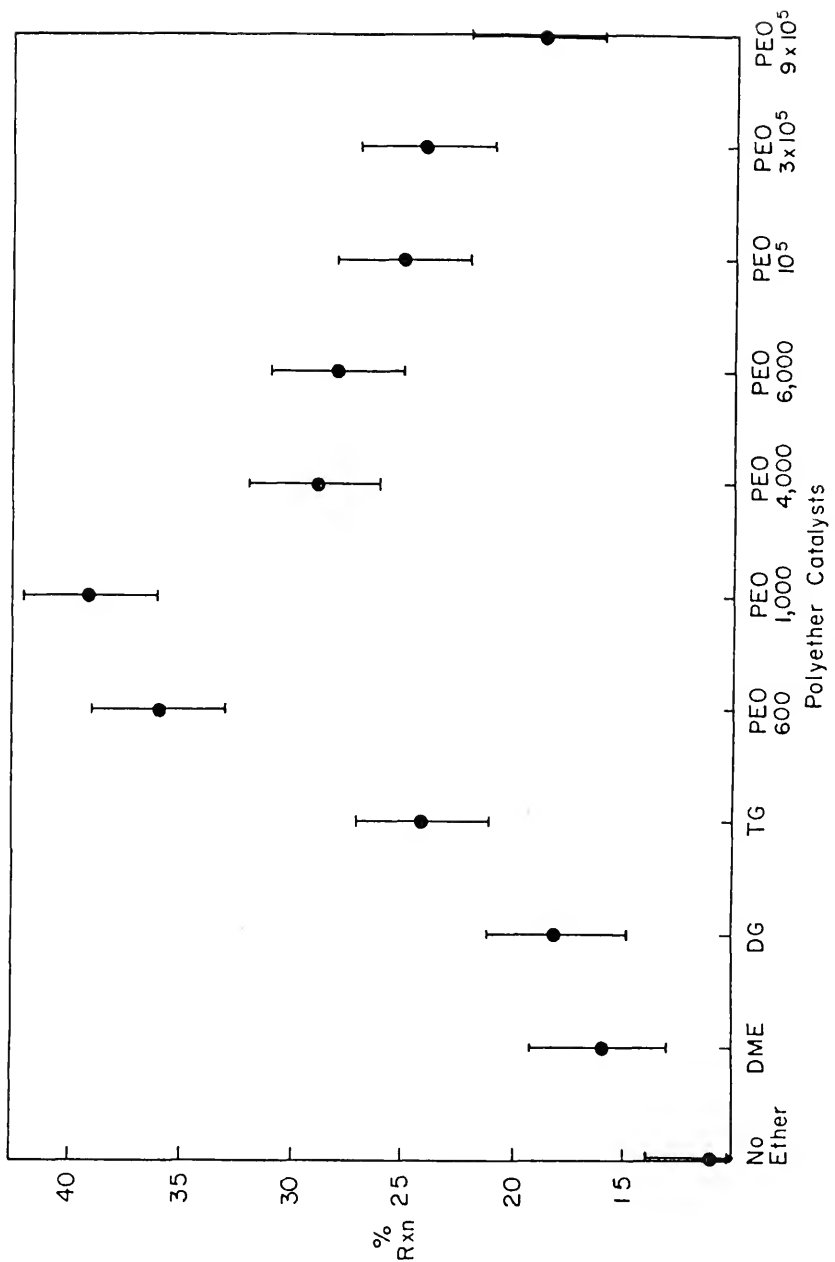


Figure 24. Butyl Bromide + Sodium Acetate in CH₃CN After 3 Days

In order to determine the relative catalytic ability of the various molecular weight PEO polymers and P(PHD) with respect to crown ethers, the reaction was run in the presence of 18-crown-6 and the polymeric crown ether, poly(vinylbenzo-15-crown-5). Due to the ability of these materials to selectively complex potassium ions over sodium ions,⁴² the reactions were also run with the potassium salt. The results are given in Table 17.

Table 17. Catalysis of 3.7×10^{-2} M Butyl Bromide + 9.6×10^{-2} M Sodium and Potassium Acetate in Acetonitrile

Ligand	[Ligand] in monomer	Salt	Rxn. Time	Percent Rxn.
18-crown-6	4.0×10^{-2}	NaOAc	3 days	81
	4.0×10^{-2}	KOAc	3 days	92
Poly(vinylbenzo-15-crown-5)	4.0×10^{-2}	NaOAc	3 days	75
	4.0×10^{-2}	KOAc	3 days	90
P(PHD)	1.0	NaOAc	5 days	74
	1.0	KOAc	5 days	90

The cation effects of the P(PHD) catalyzed reaction were also examined by comparing the products

derived from sodium and potassium acetate. The results are included in Table 17.

Even with much lower ligand concentration, the powerful cation complexing agents catalyzed the reaction to a larger extent than did PEO or P(PHD) after three days. With both crown ethers, the potassium salt gave higher percent reactions.

Discussion

The variation in percent reaction with the various polyether catalysts indicates that there is an absence in leveling effects when no water is present. Also, the increase in reaction between three and four days from Table 15 indicated that no equilibrium was being approached after that length of time. Since these reactions are much slower than those in homogeneous media, failure of the crown ether solutions to go to completion may have been due to insufficient reaction time rather than an equilibrium being established.

Once again, the relatively low reactivities with the low molecular weight glymes correlate well with the argument of less favorable entropy of complexation with these polyethers which was brought out in the UV-visible and conductance studies. The variation in the catalytic ability of the poly(ethylene oxide) samples could possibly be the result of two factors. The lower molecular

weight polymers may be more efficient in their transport of salt from the crystal into the solution phase. Also, the high molecular weight polymers may complex the salt less efficiently once it is in solution. Either or both of these effects would lead to higher reactivities with the lower molecular weight polymers.

From Table 16, it may be seen that P(PHD) produces approximately the same percent yield as the low molecular weights of PEO. This agrees with the cation complexing abilities of these polymers as determined by UV-visible and conductance studies. The reaction between butyl bromide and sodium acetate in the presence of crown ethers gave results which could be predicted on the basis of the cation complexing ability of the cyclic ethers. Even small quantities of the powerful cation coordinating crown ethers gave very high yield reactions. Poly(vinylpyrrolidone), which has been shown to catalyze the Williamson reaction between sodium phenoxide and butyl bromide,⁴⁵ gave a high yield equal to the most efficient PEO polymers. Apparently, the pyrrolidone units are quite efficient in coordinating the sodium cation due to their high dipole moment.

The higher yield reactions demonstrated by potassium salts as compared to sodium salts with P(PHD) were directly opposite to the relative degree of binding of these salts determined by conductivity. This may be

compared to the higher yields with potassium salts in the presence of crown ethers which have demonstrated potassium selectivity with respect to cation binding. Although more sodium ions are bound to P(PHD), there are apparently other factors involved which reduce the interaction between the acetate and potassium ions more than with sodium ions. There should be less electrostatic interaction between potassium and acetate ions compared to the interaction between sodium and acetate ions so that the apparent higher reactivity of the complexed potassium salt is reasonable.

CHAPTER IV

EXPERIMENTAL PROCEDURES

Preparation and Purification of Materials

Solvents

In most cases, the solvents used were reagent analytical grade and were not further purified. Those solvents used in UV-visible spectrometry or conductance were measured before use to ensure that they would not interfere with sample measurements. Acetonitrile used in the polymer catalysis reactions was distilled from CaH_2 and stored over molecular sieves to reduce the moisture content.

Glymes, PEO, and PVP

Dimethoxyethane, bis(2-methoxyethyl)ether or diglyme, and bis[2-(2-methoxyethoxy)ethyl]ether or tetraglyme were all commercially available and were distilled under vacuum prior to use. The low molecular weight poly(ethylene oxide) samples including PEO 600, PEO 1000, PEO 4000, and PEO 6000 were obtained from Union Carbide under the trade name Carbowax. The higher

molecular weight poly(ethylene oxide) samples including PEO 10^5 , PEO 3×10^5 , PEO 9×10^5 , and PEO 6×10^6 were also available from Union Carbide under the name Polyox. All of the poly(ethylene oxide) samples were used without further purification. Poly(vinylpyrrolidone), molecular weight 40,000, was obtained from Polysciences, Inc.

Vinyl Glyme

The vinyl glyme 3,6,9,12,15-pentaoxa-1-heptadecene was obtained from Aldrich. Approximately 100 ml of monomer were polymerized by adding a small drop of distilled $\text{BF}_3 \cdot \text{OEt}_2$ to the monomer in a 250 ml round-bottom flask. The system was kept under nitrogen and periodically shaken for approximately one week. The resulting polymer was soluble in virtually all common solvents. The sample was placed under vacuum (0.05 mm) at approximately 80°C to remove any unreacted monomer. The absence of monomer was confirmed by IR analysis. A slight yellow color was present which was removed by dissolving the polymer in CHCl_3 and passing this solution through a column of 1:1 diatomaceous earth and charcoal. The molecular weight was measured on a Mechrolab Model 502 High Speed Membrane Osmometer and was found to be 40,000.

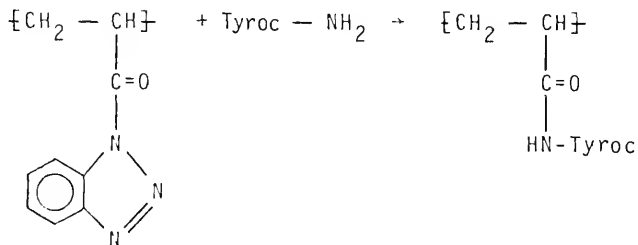
Crown Ethers

Dicyclohexyl-18-crown-6 was obtained from Dr. H. K. Frensdorff of E. I. duPont de Nemours Elastomers

Department and recrystallized from petroleum ether. The nonsubstituted crown ether, 18-crown-6, was purchased from PCR, Inc. Purification was accomplished according to the method of Gokel *et al.*⁷⁶ Poly(vinylbenzo-15-crown-5) was obtained from Dr. J. Smid, SUNY, Syracuse, and was used without further purification.

Antibiotic Compounds

The antibiotic tyrocidine was obtained in the HCl form from ICN Pharmaceuticals, Inc. as a mixture of at least five separate compounds. These components varied in the amino acids present at three of the ten positions of the cyclic peptide. None of the available separation techniques was successful in separating these components. As a result, the antibiotic was used as the mixture. Poly(acryloyltyrocidine) was synthesized by the following reaction:



where Tyr-NH₂ is the ornithine amine group.

This synthesis first required the synthesis of poly(acryloylbenzotriazole). Practical grade benzotriazole was recrystallized by melting 95 g of crude material over a hot flame and adding the molten material into 300 ml of benzene. The solution was stirred until crystallization began. The solution was chilled for two hours and filtered.⁷⁷

A solution of 48 g benzotriazole, 60 ml of dry triethylamine, and 600 ml of dry benzene was added dropwise to a well-stirred solution of 32 ml acryloyl chloride in 200 ml of dry toluene. The reaction mixture was kept between -5° and 0°C by external cooling with a dry ice-isopropanol bath. The reaction mixture was continuously stirred while it was allowed to warm to room temperature over a two-hour period. The solution was filtered, and the filtrate was extracted with cold water and with a saturated solution of sodium chloride. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to dryness under vacuum after adding 0.5 g of t-butyl catechol. The temperature was never allowed to rise above 30°C during evaporation. The residue was a yellow, flaky material. Some losses, due to polymerization, were often encountered during recrystallizations, and the preferred procedure was to treat the crude product with n-heptane preheated to 80°C, filter, and cool the filtrate rapidly in a dry ice-isopropanol bath. The precipitate was 14 g

of a white, powdery solid, m.p. 65-67°C. The literature value was 67-68°C.⁷⁸

Poly(acryloylbenzotriazole) was made by placing 10 g of monomer in 30 ml of dry benzene into a 50 ml round-bottom flask, adding 50 mg of azobisisobutyronitrile, and purging with nitrogen. The flask was then kept at 65-70°C for approximately 10 hours. The polymer precipitated, was collected, and dissolved in methylene chloride. The polymer was then reprecipitated in an excess of anhydrous ether and dried under vacuum. The yield was 23%. The IR spectrum of poly(acryloylbenzotriazole) is given in Figure 25. It matched the infrared spectrum given by Ferruti *et al.*⁷⁸

The attachment of the antibiotic tyrocidine to poly(acryloylbenzotriazole) presented possible cross-linking problems due to two reactive sites on the antibiotic, the ornithine primary amine and the tyrosine phenolic group. The tyrosine function was acylated by dissolving tyrocidine·HCl in an equal volume mixture of acetic acid and acetic anhydride and stirring for four hours. The acetic acid and unreacted acetic anhydride were then removed by vacuum distillation. The product was a light brown, powdery solid. The HCl on the ornithine amino acid blocked this position. The HCl could then be removed with Et₃N in order to provide a nucleophilic site.

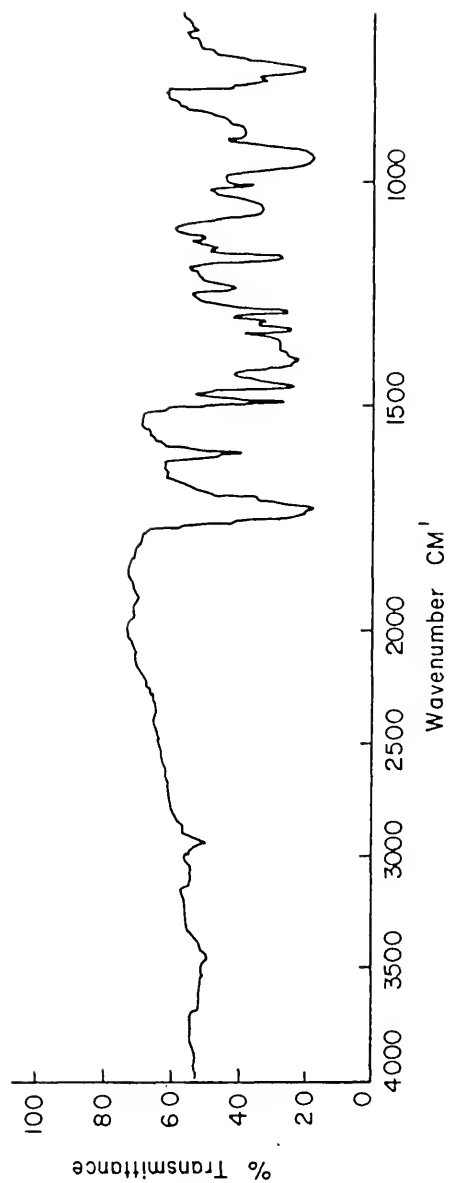


Figure 25. Infrared Spectrum of Poly(acryloylbenzotriazole)

Poly(acryloyltyrocidine) was prepared by adding 2.0 g poly(acryloylbenzotriazole) to 0.4 g of acylated tyrocidine and 3.0 ml triethylamine in 35 ml of chloroform. The mixture was stirred for two days at 60°C. At this time 8 ml of propylamine was added to cleave unreacted benzotriazole units in order to prevent hydrolysis and possible polyelectrolyte formation. The mixture was stirred for an additional day at 60°C. Chloroform and triethylamine were removed by rotary evaporation. The remaining solid was added to a small amount of chloroform and filtered to remove unreacted tyrocidine and the byproduct $\text{Et}_3\text{N}\cdot\text{HCl}$. The polymer was then precipitated in ether. The product was 0.6 g of flaky, light brown material. The UV spectrum indicated a tyrocidine absorption at 280 nm with no indication of benzotriazole at 251 nm (Figure 26). Assuming that the components of the antibiotic reacted in the same percentage in which they were present in the initial mixture, the absorption of the polymer was compared to that of tyrocidine itself and it was determined that the product contained one antibiotic molecule for every 12 monomer units.

Salts

Most of the salts studied, such as NaCl, KCl, KBr, NaBPh_4 , and NaOAc, were all available in analytical

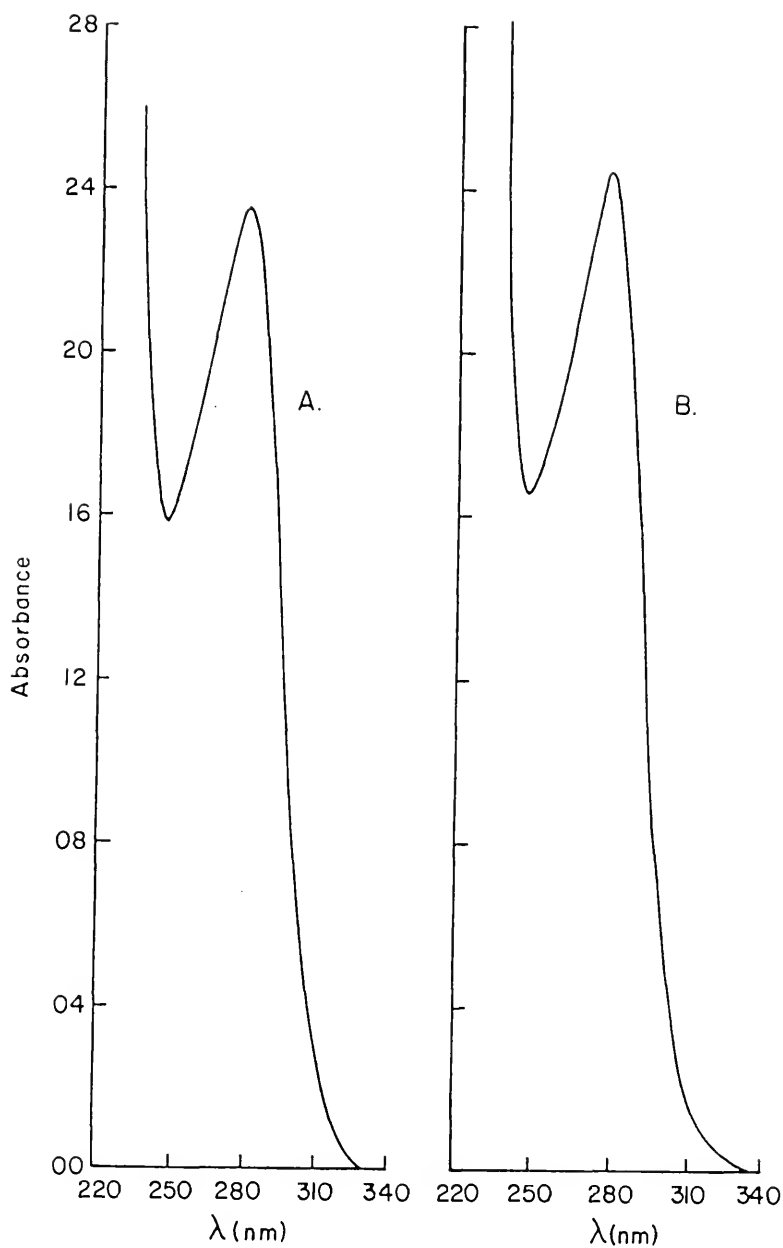


Figure 26. Absorption of (A) Tyrocidine·HCl; (B) Poly(acryloyl-tyrocidine) in Methanol

reagent grade. They were dried overnight at 0.5 mm prior to use.

KBPh_4 was made by treating a dilute aqueous solution of sodium tetraphenylboride with a dilute aqueous solution of KCl . The insoluble KBPh_4 precipitated, was filtered, washed, and recrystallized from 1:3 water-acetone.⁷⁹ Bu_4NBPh_4 was made in a similar manner by adding a 2% aqueous solution of NaBPh_4 to a 2% aqueous solution of Bu_4NI . The precipitate was washed with water after filtering, recrystallized from a 1:3 water-acetone mixture and dried for three days under vacuum at room temperature.⁸⁰

The picrate salts of Na, K, and Cs ions were all prepared by neutralizing picric acid with the appropriate alkali hydroxide in ethanol. The products were recrystallized from absolute ethanol and dried at room temperature for two days at 0.01 mm.

Cation Binding Measurements

Viscometry

The polymer solution was made by adding PEO 6×10^6 to methanol to form 100 ml of a saturated solution. This solution was allowed to stand for two days, was decanted, centrifuged, decanted again and diluted to 1 liter. This method was used because vigorous stirring

of the polymer solutions would lead to mechanical degradation. The concentration was determined by evaporating the solvent from 10 ml samples and weighing the remaining polymer. The concentration was found to be 1.10 g/l. Appropriate quantities of salts were added to the polymer prior to viscosity determinations. The viscosity measurements were made with a Cannon Viscometer Number 25-K632 in a constant temperature water bath at 25.0°C.

Distribution Equilibria

Distribution equilibria studies involving the extraction of alkali picrate salts from an aqueous layer into an organic layer containing poly(acryloyltyrocidine) were followed by UV-visible spectroscopy due to the absorption of the picrate anion at ~ 360 nm in CHCl_3 . The reported extinction coefficient of this absorption is $1.65 \times 10^4 \text{ cm}^{-1} \text{ M}^{-1}$.⁴⁴ The spectra were taken on a Beckman ACTA V Spectrophotometer.

The aqueous layers consisted of $1.0 \times 10^{-3} \text{ M}$ picrate salt and $5.0 \times 10^{-2} \text{ M}$ of the corresponding alkali chloride. The presence of the chloride served to increase the ionic strength of the aqueous layer to prevent intermixing of the aqueous and chloroform layers and to increase the transfer of metal salt into the organic layer to increase complexation. The chloroform layer contained

sufficient poly(acryloyltyrocidine) for the solution to have an estimated tyrocidine concentration of 1.3×10^{-3} M.

Twenty ml of each solution were placed in a stoppered 50 ml Erlenmeyer flask and shaken periodically for approximately one day. The picrate absorption in the CHCl_3 layer was then measured and compared to a blank sample which contained no polymer. The concentration of salt extracted was calculated using the reported extinction coefficient.

Potentiometry

Potentiometry involving the use of ion-selective electrodes was used to follow the process of cation complexation by PEO.⁶ The electrodes used were Corning Monovalent Cation Electrode (Catalog Number 476220) for potassium ions, Corning Sodium Ion Electrode (Catalog Number 476210) for sodium ions, and an Ag/AgCl reference electrode made by Dr. M. Mohan from this department. This reference electrode necessitated the use of alkali chloride salts due to possible electrode contamination with other anions. The potential was measured with a Corning Digital 112 Research pH meter. In order to measure solution potentials in methanol, it was necessary to condition the glass electrodes stepwise in aqueous methanol solutions containing greater percentages of methanol until the electrode was finally in pure methanol.

A closed glass cell with two openings for the electrodes, which were sealed by serum caps, was used for the measurements. The 25 ml solutions were stirred by a small magnetic stirring bar after addition of solid ligand until the ligand had dissolved. Stirring was then discontinued, and readings were taken at one minute intervals until the readings differed by no more than 0.2 mV.

Calibration curves of $[MCl]$ vs. emf were measured for $[MCl]$ from 1.0×10^{-5} to 1.0×10^{-2} . This gave the potential for free ions in solution. Then when PEO was added to a salt solution, the emf value was compared to the calibration curve to obtain the concentration of free ions remaining in solution. This procedure was checked for NaCl plus dicyclohexyl-18-crown-6 and 18-crown-6 and was found to reproduce literature values.⁶

UV-visible Spectrometry

The change in the absorption spectra of sodium picrate in 10% THF/90% $CHCl_3$ upon addition of polyethers was measured by the Beckman ACTA V Spectrometer. The addition of THF was necessary in order to dissolve sufficient concentration of sodium picrate in $CHCl_3$ but this had no effect on the absorption spectra.

The change in λ_{max} of sodium picrate with respect to tetraglyme concentration was measured by titrating 100 ml of 1.0×10^{-4} M sodium picrate with 1.0×10^{-2} M

tetraglyme plus 1.0×10^{-4} M sodium picrate in 10% THF/90% CHCl_3 . This kept the picrate concentration constant while increasing the tetraglyme concentration. The absorption was measured after each tetraglyme addition.

The absorption spectra of 1.0×10^{-4} M sodium picrate in the presence of 1.0×10^{-4} M and 1.0×10^{-3} M polyethers were measured as follows. A 1.0 liter stock solution of 1.0×10^{-4} M sodium picrate was prepared. From this solution, 50 ml solutions of 1.0×10^{-3} M polyether plus 1.0×10^{-4} M sodium picrate were prepared. Diluting these solutions by a factor of 10 with the 1.0×10^{-4} M stock solution of sodium picrate gave solutions of 1.0×10^{-4} M sodium picrate plus 1.0×10^{-4} M polyether.

Conductance

The conductivity experiments were carried out by adding various polyethers to 15 ml of 1.0×10^{-4} M tetraphenylboride salts in acetone, tetrahydrofuran, and acetonitrile at 25°C. The cell constant for the particular cell used was 0.1159. For the low concentrations of polyether, approximately 4.0×10^{-4} M to 5×10^{-3} M in monomer, the additions were made by titration in which the titrant contained the polyether and the same concentration of tetraphenylboride salt that was being titrated. Therefore, the solution in the conductance cell always

contained the same concentration of tetraphenylboride salt but varied in polyether concentration. The higher polyether concentrations, 1.1×10^{-3} M to 1.0×10^{-1} M in monomer, involved the direct addition of solid polymer to the NaBPh_4 solution.

After each addition of polyether, the conductance was determined by a General Radio 1673-A Automatic Capacitance Bridge operating at 1 KHz. This was connected to a General Radio 1672-A Digital Control Unit also operating at 1 KHz.

Reactions

Reaction Methods

The catalytic reactions were all carried out in 5 ml round-bottom flasks with a side arm stoppered with a septum cap. The side arm allowed withdrawal of small amounts of solution for gas chromatographic analysis without interrupting the reaction. The flasks were connected to condensers and drying tubes. These systems were grouped in series of five, supported by a metal rack, and immersed in an oil bath. The oil baths were maintained at $\sim 100^\circ\text{C}$ to ensure sufficient refluxing of the acetonitrile solutions.

For each reaction, 0.02 g of alkali acetate salt, the polyether, and 2.5 ml acetonitrile were added to the

round-bottom flask and refluxed for 30 minutes. This was followed by the addition of 10 μ l of butyl bromide with a syringe. For homogeneous reactions, the salt was added first followed by 0.13 ml H_2O and the flask was then swirled to dissolve the salt. The sequence was continued as above. On many of the homogeneous reactions, 10 μ l of chlorobenzene were added with the butyl bromide as an internal standard because of interference of water with the butyl bromide peak in the GC analysis. The reactions were allowed to proceed for time intervals varying from five hours to five days.

Product Analysis

Product analysis was made on a Hewlett Packard 700 Laboratory Chromatograph. The column was packed with 15% UCON 50 LB 550 X on Chromosorb G. The instrument conditions were attenuation, 1; column temperature, 90°C; injection port, 160°; detector, 182°; helium pressure, 20 lbs in⁻². The injection port was packed with glass wool in order to prevent polymers from the solution from becoming pyrolyzed in the end of the column.

For analysis of the reaction mixtures, 20-30 μ l of solution were injected onto the column. Peak areas were measured by a K and E 62 0000 Compensating Polar Planimeter.

The instrument was calibrated by injecting equal molar quantities of butyl bromide and butyl acetate into the column. The relative size of the peaks gave a correction which, when applied to acetate peaks on the product traces, gave the relative amounts of butyl bromide and butyl acetate present in the mixture. Division of the size of the corrected acetate peak by the total of the two peaks gave the percent yield. For the homogeneous system, the chlorobenzene peak was used to determine how large the bromide peak would have been had it not been obscured by water.

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BIOGRAPHICAL SKETCH

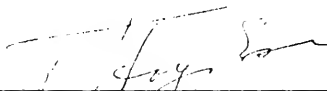
Ronald E. Cambron was born July 6, 1948 in Jackson, Tennessee. After graduation from Jackson High School, he entered the University of Tennessee at Knoxville, where he received a Bachelor of Science degree in chemistry in 1971.

While at the University of Tennessee, Mr. Cambron was enrolled in the Cooperative Education program with assignment to the Tennessee Valley Authority in Muscle Shoals, Alabama. He also served as an analytical chemist for the Water Quality Control Branch of the Tennessee Public Health Department for two summers. During his junior year, he received the Analytical Chemistry Award from the Department of Chemistry.

In September 1971, he entered the Graduate School of the University of Florida. During his first year, he was the recipient of a graduate school fellowship.

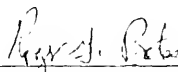
Mr. Cambron is married to Dr. Nelda H. Cambron, who is currently an assistant professor in Educational Administration at the University of Florida.

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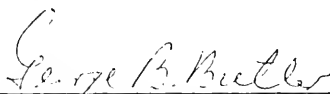
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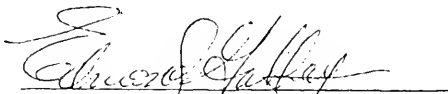
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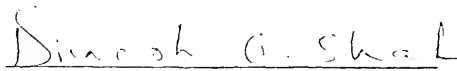


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This dissertation was submitted to the Graduate Faculty of the Department of Chemistry in the College of Arts and Sciences and to the Graduate Council, and was accepted as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

December, 1976

Dean, Graduate School

UNIVERSITY OF FLORIDA



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